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THE INSENSIBLE LOSS IN SURGICAL PATIENTS

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SINCE the incidence of reactions to parenteral fluids has been reduced, their value in the treatment of surgical patients has rapidly increased. Although parenteral fluids are widely used today, their administration still remains largely empirical. In order to determine the exact fluid requirements of surgical patients, Coller and Maddock^{1, 2, 3} proposed the clinical use of a water balance method described by Soderstrom and DuBois,⁴ and by Newburgh, Johnston and Falcon-Lesses.⁵ This, essentially, is as follows:

INCREMENTS OF WATER EXCHANGE

Available Water	Excreted Water
(1) Exogenous	(1) Perceptible
(a) Diet	(a) Urine
(b) Water as such	(b) Feces
	(c) Emesis
(2) Endogenous	(d) Drainage
(a) Oxidation	(e) Perspiration
(b) Preformed	
	(2) Insensible

Coller and Maddock³ have discussed in detail the water balance method. They emphasized especially the importance of the insensible water loss and the necessity of its replacement in the postoperative period. It is this loss which is usually overlooked clinically and which is given further study here.

Benedict and Root⁶ define insensible loss as "The gaseous emanations from the body which do not appear in the form of a sensible moisture or sweat, in other words, the insensible, invisible, intangible but weighable gaseous and vapor productions arising from the lungs in the process of exhalation and from the skin by due process of vaporization." These emanations are chiefly carbon dioxide and water vapor.

Johnston and Newburgh⁷ have shown that the insensible weight loss is the resultant of the weight of water lost by vaporization, the weight of the exhaled carbon dioxide, and the weight of the absorbed oxygen, expressed by the following equations:

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$$\text{INSENSIBLE WEIGHT LOSS} = \text{WATER VAPOR} + \text{CO}_2 - \text{O}_2$$

OR

$$\text{INSENSIBLE WEIGHT LOSS} - \text{CO}_2 + \text{O}_2 = \text{WATER VAPOR}$$

The greater proportion of the insensible weight loss is composed of water. According to Benedict and Root⁶ it is about 85 per cent, and to Newburgh, *et al*,⁸ the water vapor varies from 85 to 100 per cent of the insensible loss, depending upon the amount of carbohydrate, protein and fat being metabolized.

Newburgh and his associates^{8,9} have determined that 25 per cent of the total body heat was removed by the vaporization of water. In another study¹⁰ they could demonstrate no reduction in the amount of water vaporized when dehydration of as much as 6 per cent of the total body weight had been produced. It appears, therefore, that the weight of the vaporized water is proportional to the total energy exchange of the body and is not influenced by lesser degrees of dehydration.

Recorded determinations³ of insensible loss in surgical patients vary from 1,000 to 2,500 Gm daily, whereas the recorded average⁸ losses of normal adults at normal activity vary between 1,000 and 1,500 Gm daily. It would seem that the total energy exchange of normal active adults would be greater than surgical patients confined to bed, and in view of the above work the insensible loss of the active adults should be greater. Because of this apparent contradiction and the clinical importance of this form of fluid loss, it was felt that further study of the insensible loss in surgical patients was indicated.

The Method and the Control—In a study of sick surgical patients the method must be adapted to the welfare of the patient and at the same time record the effect of changing intrinsic and extrinsic conditions. An indirect method described by Wiley and Newburgh¹¹ was, therefore, used in this study. The method is summarized by the following mathematical equations:

$$\begin{array}{c} \text{INITIAL WEIGHT} + \text{TOTAL INTAKE} \\ \text{minus} \\ \text{PERCEPTIBLE OUTPUT} + \text{FINAL WEIGHT} \\ \text{equals} \\ \text{INSENSIBLE LOSS} \end{array}$$

The patients were weighed daily at the same hour on a silk balance accurate to ± 5 Gm. All intake and output was weighed and careful watch was maintained so that nothing was lost before weighing. Weights were measured and checked by more than one observer before recording. Insensible loss and sweating are two distinct and independent processes,^{6,12,13} hence perspiration was carefully separated from the insensible loss. Bedding and clothing were weighed dry and as soon as perceptible moisture appeared, they were weighed again to determine the loss due to sweat. An effort was made to avoid sweating* by discarding all excess bedding. In the immediate postoperative period,

* Newburgh, *et al*⁸ have shown that the temperature and the humidity of the environment had little effect on the insensible loss when the subject was clothed and comfortable. All studies were made during the winter and early spring months.

when sweating is apt to occur, the patients were protected from drafts and kept comfortably covered

Since such factors as body temperature, activity in bed and caloric exchange could not be controlled in the sick surgical patient, determinations were made over several 24-hour periods. The more prolonged observations reflect the result of changing conditions, and in combination give a record of insensible loss under average surgical conditions. Although the insensible loss varies from day to day,¹⁴ the losses of any one case on various days will be found to

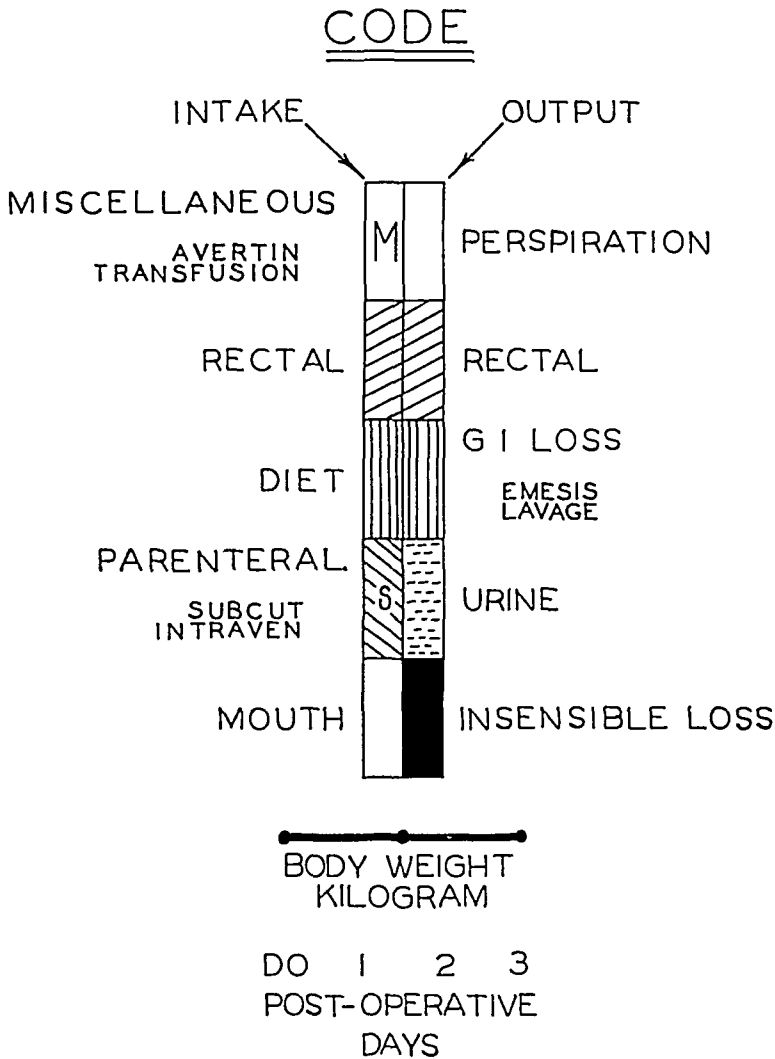


CHART 1—The Code. Each column represents a 24 hour period. The left hand portion is divided into the increments of intake, the right hand portion into the increments of output. The solid black line represents the cumulative effect of daily fluctuations in body weight.

fall within a small range of fluctuation. Rather wide variations occur on only a few days and these will be discussed separately.

As previously pointed out, the percentage of water vapor in the total insensible weight loss varies with the carbohydrate, protein and fat being oxidized. The amount and proportion of these substances oxidized varies from day to day. Under surgical conditions the mixture oxidized and the weight of the CO₂ and O₂ could not be ascertained. Hence all losses recorded are losses of insensible weight. From a clinical standpoint, the insensible weight loss

may be considered as water loss, as the difference between the two, due to the CO_2 and O_2 exchange, is relatively small

Observations and Data—All determinations were graphed on the same scale, the code (Chart 1) describing the various increments

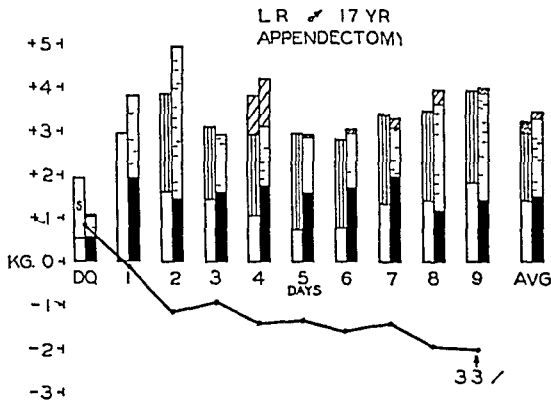


CHART 2—Case L R (P H No 269427) Acute Appendicitis

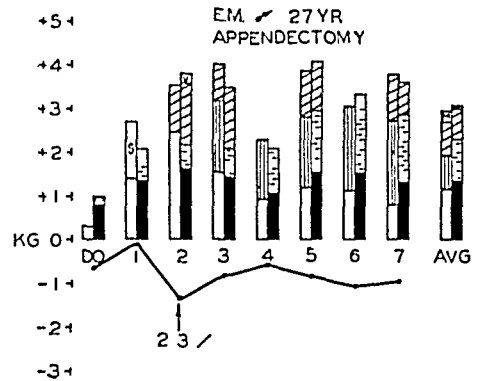


CHART 3—Case E M (P H No 510618) Acute Appendicitis

Case L R—(P H No 269427) Acute Appendicitis. There was a rapid post operative recovery. The maximum temperature^{*} of 100.8° F occurred on the second day. The weight loss continued to 33 per cent of the original body weight in spite of a good caloric intake the last seven days. The average insensible loss was 1,503 Gm per day. The loss on the day of operation does not represent a full 24 hour period (Chart 2).

Case E M—(P H No 510618) Acute Appendicitis. The postoperative course was uncomplicated. The temperature curve reached a maximum of 101.8° F on the first day. The average daily insensible loss was 1,341 Gm (Chart 3).

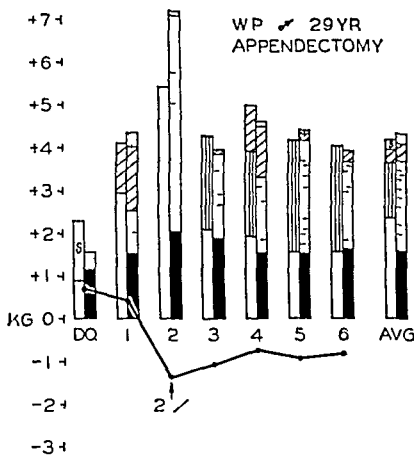


CHART 4—Case W P (P H No 318340) Recurrent Appendicitis

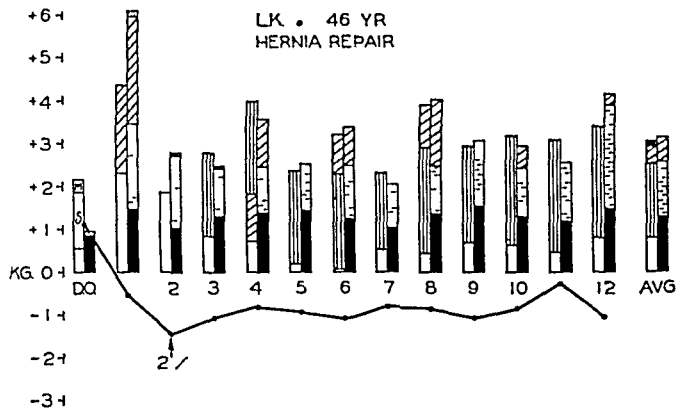


CHART 5—Case L K (P H No 509519) Left indirect inguinal hernia

Case W P—(P H No 318340) Recurrent Appendicitis. The patient had a smooth postoperative course with moderate perspiration the first two days but slight thereafter. The cumulative body weight loss reached a maximum of 2 per cent on the second day coincident with a large fluid intake by mouth and a diuresis of 5,090 Gm. The maximum insensible loss of 2,034 Gm occurred on the same day. The average daily insensible loss was 1,638 Gm (Chart 4).

* All temperatures recorded were obtained per rectum

Case L K—(P H No 509519) Left Indirect Inguinal Hernia The postoperative course was uncomplicated The maximum temperature, of 101° F, occurred on the first day The insensible loss averaged 1,256 Gm per day (Chart 5)

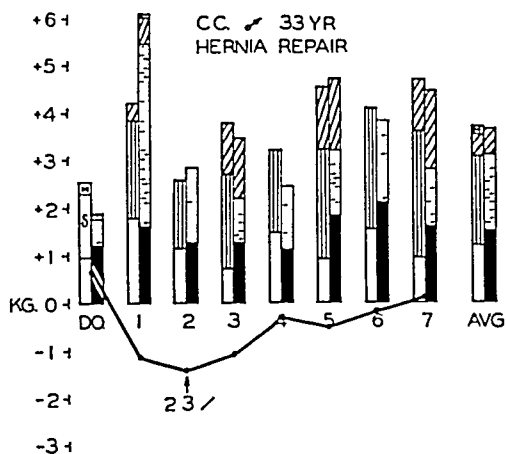


CHART 6—Case C C (P H No 505551) Bilateral inguinal hernia, duodenal ulcer, left herniorrhaphy

high caloric intake and increased activity in bed The average daily insensible loss was 1,665 Gm The average for both operations, covering a period of 22 days, was 1,604 Gm (Chart 7)

Case C C—(P H No 505551) Bilateral Inguinal Hernia, Duodenal Ulcer, Left Herniorrhaphy There was a minimal postoperative reaction with the maximum temperature, of 100.8° F, occurring on the first day Maximum body weight loss of 2.3 per cent followed a diuresis on the first day of 3,860 Gm The insensible loss which averaged 1,498 Gm per day was somewhat higher the last three days when the caloric intake averaged over 2,900 calories per day (Chart 6)

Case C C—(P H No 505551) Right Herniorrhaphy second operation (ref Chart 6) There was practically no postoperative reaction A diuresis of 3,400 Gm on the first day was followed by the maximum body weight loss, of 2.5 per cent Again the insensible loss was slightly higher on the last four days, during a period of

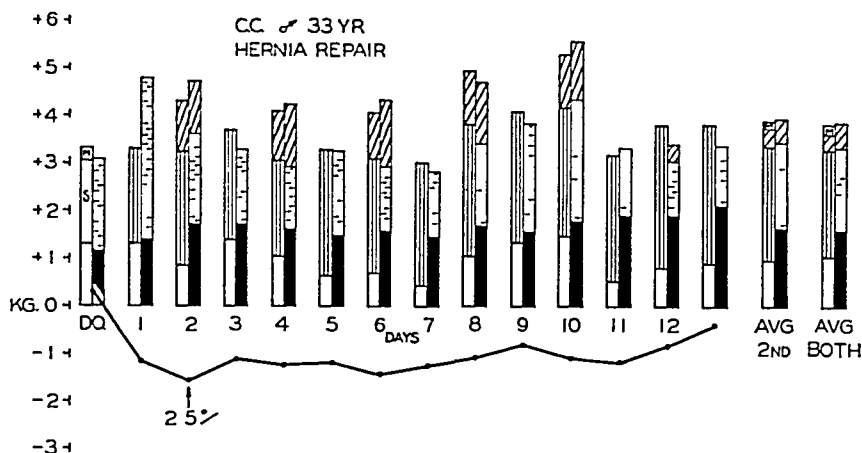


CHART 7—Case C C (P H No 505551) Second operation (ref Chart 6) Right herniorrhaphy

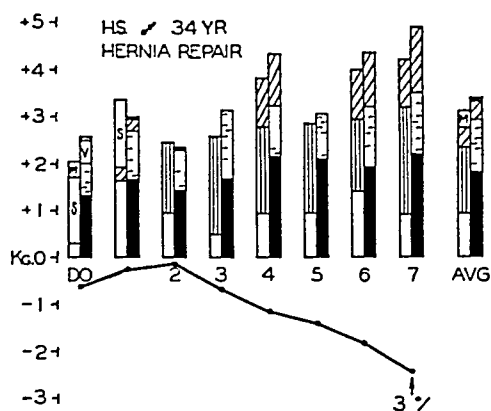


CHART 8—Case H S (P H No 507115) Bilateral inguinal hernia, right herniorrhaphy

Case H S—(P H No 507115) Bilateral Inguinal Hernia, Right Herniorrhaphy There was a mild postoperative reaction The maximum temperature, of 101.8° F, occurred on the first day There was progressive loss of 3 per cent of the original body weight The average daily insensible loss for the period was 1,804 Gm (Chart 8)

Case H S—(P H No 507115) Left Herniorrhaphy second operation (ref Chart 8) There was a minimal postoperative reaction with the maximum temperature, of 99.8° F, occurring on the first day There was a slow progressive loss of 4.6 per cent of the original body weight even though the caloric intake averaged 2,785 calories

for the last eight days. The average daily insensible loss for the second operation was 1,845 Gm and for both operations, a period of 22 days, 1,830 Gm (Chart 9)

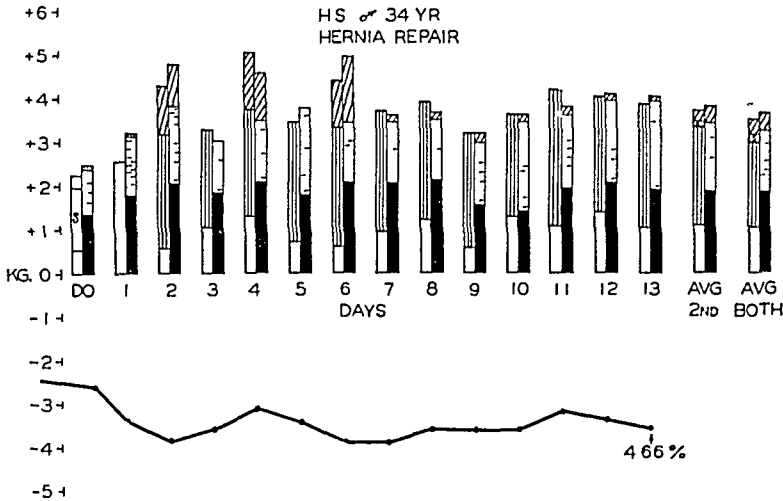


CHART 9 —Case H S (P H No 507115) Second operation (ref Chart 8)
Left herniorrhaphy

Case F M —(P H No 493334) Cholecystectomy, Appendicectomy. There was a moderate postoperative reaction the first three days with slight perspiration on the first day. The maximum temperature was 102.8° F. There was a gain of 1,730 Gm in weight the first two days. This was probably due to water retention as the urinary output was low. On the third day the urinary output increased, the insensible loss was high and the weight started to decrease to a maximum loss of 3.6 per cent. The insensible loss was high on the third and thirteenth days. The average daily insensible loss for the 15 days was 1,500 Gm (Chart 10)

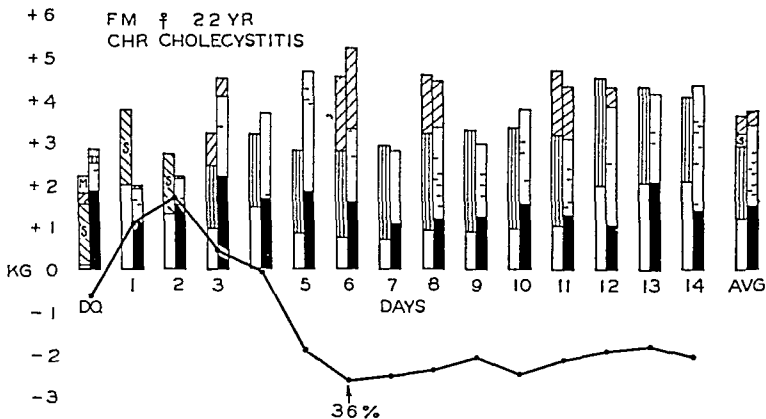


CHART 10 —Case F M (P H No 493334) Cholecystectomy,
appendicectomy

Case E B —(P H No 517132) Partial Thyroidectomy. This patient presented clinical signs and symptoms of hyperthyroidism with an elevated basal metabolic rate. There was clinical improvement during the preoperative period associated with a small gain in weight. On the day of operation there was a gain in weight of 1,780 Gm. This was probably due to retention for as the urinary output increased on the following day to 3,060 Gm the body weight decreased 1,920 Gm. The large intake and output on the first day was due to a cool colonic lavage given for a rising temperature, the maximum of which was 102.4° F. The further course was uneventful and the basal metabolic rate

INSENSIBLE LOSS IN SURGICAL PATIENTS

on the sixth day was plus four. The daily average insensible loss for the preoperative period was 1,467 Gm, for the postoperative period 1,321 Gm, and for the 15 day period the average was 1,399 Gm (Chart 11)

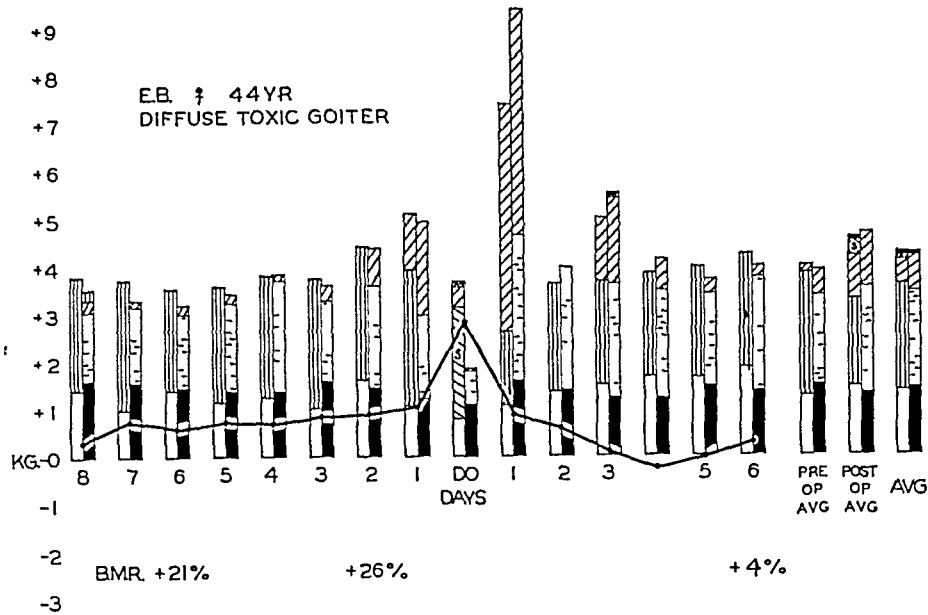


CHART 11—Case E. B. (P. H. 517132) Partial thyroidectomy

Case I E—(P. H. No 512999) Partial Thyroidectomy. This was the postoperative study of an uncomplicated thyroidectomy performed for a diffuse toxic goiter. The basal metabolic rate three days before operation was plus 36. The maximum temperature was 100.4° F on the first day. The basal metabolic rate on the seventh postoperative day was plus three. The daily average insensible loss was 1,154 Gm (Chart 12)

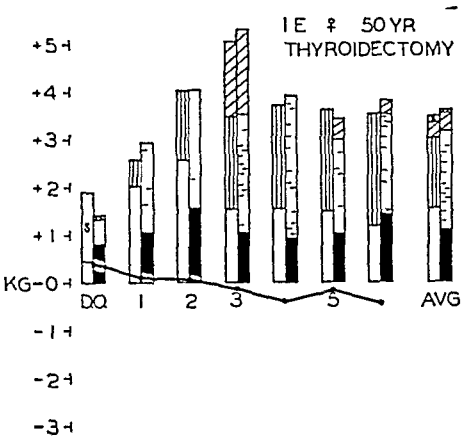


CHART 12—Case I. E. (P. H. No 512999) Partial thyroidectomy

Case E H—(P. H. No 302641) Partial Thyroidectomy. This case presented typical signs and symptoms of hyperthyroidism. The initial basal metabolic rate was plus 47, and the insensible loss 2,258 Gm. These decreased before operation to plus 27 and 1,610 Gm, respectively. There was a slight postoperative reaction, the maximum temperature reaching 101.8° F on the second day. On the fifth day the patient became emotionally upset. The insensible loss on this day was increased and the basal metabolic rate at the end of the 24 hour period was plus 16. The preoperative daily insensible loss averaged 1,889 Gm. The postoperative daily insensible loss averaged 1,244 Gm. The average daily loss for the 16 days was 1,647 Gm (Chart 13)

Case P P—(P. H. No 503254) Exploratory Celiotomy, Biopsy of Pylorus, Anterior Gastrojejunostomy. There was a moderate reaction during the first few postoperative days with an uneventful but slow convalescence. The maximum temperature was 101.8° F on the first postoperative day.

There was a progressive gain of 13.1 per cent of the body weight up to the fourth postoperative day. This was associated with a low urinary output, gastric retention and peripheral edema. At the same time the patient was thirsty and the tongue and skin were dry. There was evidence of hemoconcentration as shown by the increasing hematocrit, plasma specific gravity and plasma proteins determinations.

Parenteral fluids for six days consisted of physiologic saline and Ringer's solutions. There was definite salt retention until the fourth postoperative day, even though

the urinary chlorides, as determined by the Mohr¹⁵ test, as discussed by Fantus,¹⁰ increased to 24 per cent. On the fifth day, following administration of 5 per cent dextrose solution, improvement took place as evidenced by loss in weight, increase in the urinary output, disappearance of edema and reduction in hematocrit and specific gravity determinations. Furthermore, all clinical evidences of dehydration disappeared.

It is felt that adequate fluids were administered but the patient received an excessive amount of sodium ions, consequently fluid was retained in the tissues^{17, 18, 19, 20}. The gastric retention may also be attributed to edema of the gastrojejunostomy stoma and intes-

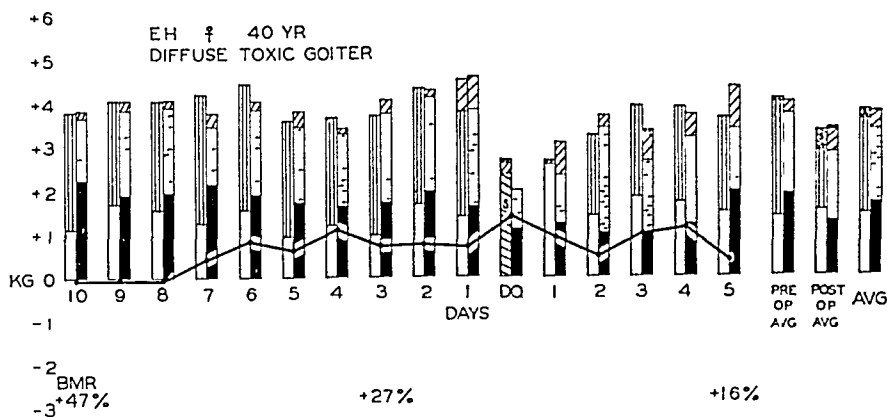


CHART 13—Case E H (P H No 302641) Partial thyroidectomy

tinal wall as described by McCray, Barden and Ravdin²¹. Coller and Maddock,²² and Nadler²³ have discussed in detail the relative value of fluids in surgical patients.

The insensible loss averaged 1,180 Gm per day for the 21 day period (Chart 14).

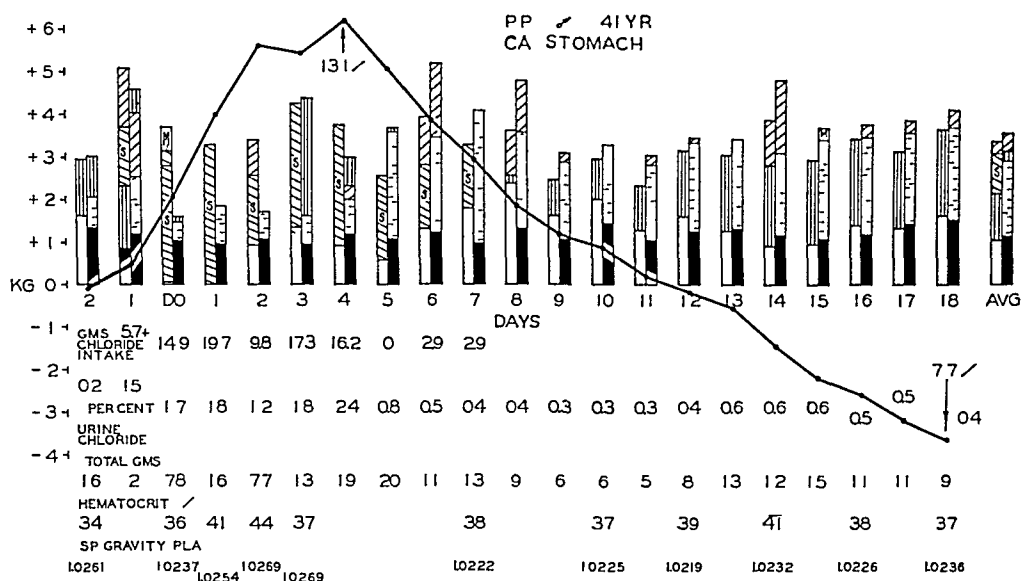


CHART 14—Case P P (P H No 503254) Exploratory celiotomy, biopsy of pylorus, anterior gastrojejunostomy

Case J T—(P H No 509921) Taking Down of Gastro-Enterostomy, Gastrorrhaphy, Partial Jejunectomy, End-to-End Jejunojejunostomy. There was a mild postoperative reaction. The maximum temperature, of 102.8° F, with but one exception occurred on the first day. The insensible loss was low on the day of operation and continued throughout the first three postoperative days during which time clinical evidences of dehydration

INSENSIBLE LOSS IN SURGICAL PATIENTS

were present Manchester, *et al*,²⁴ and Levine and Wyatt²⁵ have demonstrated the effect of severe dehydration in reduction of the insensible loss Newburgh and Johnston¹⁰ could demonstrate no effect on the water of vaporization by dehydration of as much as 6 per cent Hence it must be presumed that prior to this four day period the patient had lost more than 6 per cent of his body weight in fluids

On the second day, when the loss was lowest, the patient presented a typical picture of severe dehydration and passed 110 Gm of urine during the first 12 hours The pulse suddenly increased to 150 and the temperature to 104° F After an infusion there was definite clinical improvement, the pulse and temperature fell and the urinary output, for the remaining 12 hour period, was 1,020 Gm

The patient maintained his weight to the sixth postoperative day, at which time parenteral fluids containing salt were stopped and a diuresis developed Weight loss continued until the twelfth day, when it was 7.9 per cent of the body weight Sodium chloride capsules were administered by mouth and the weight slowly increased, but it was

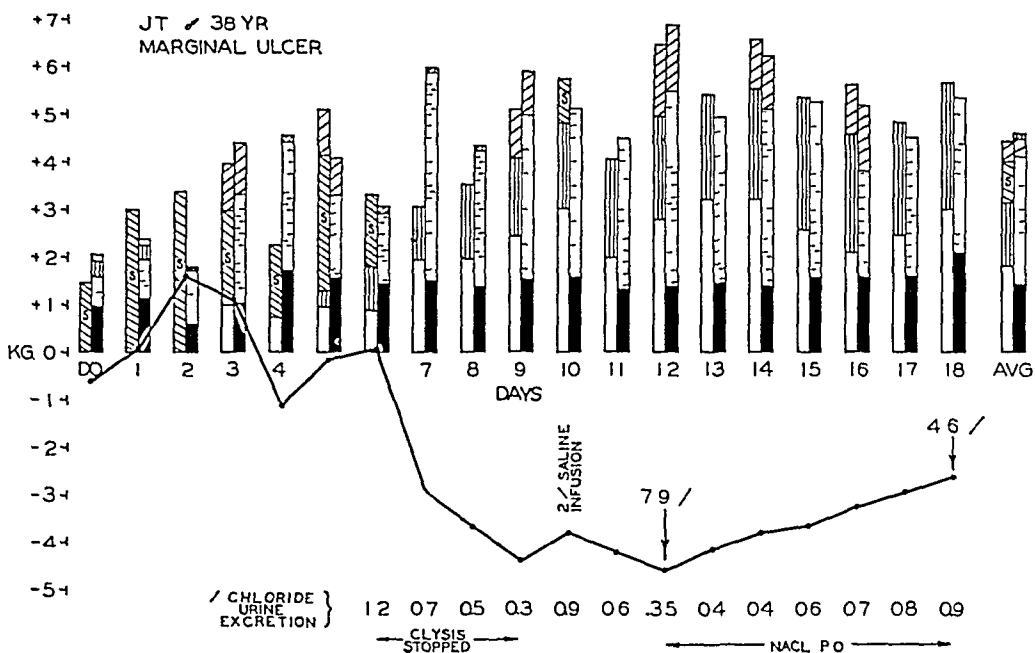


CHART 15—Case J T (P H No 509921) Taking down of gastro enterostomy, gas trorrhaphy, partial jejunectomy, end to end jejunojejunostomy

not until the sixteenth postoperative day that the diuresis stopped and the chloride excretion rose above normal

It is believed that the conditions in this case are the converse of the previous case, namely, salt starvation It might be added that for 37 days prior to operation the patient received medical treatment for the marginal ulcer during which time the nature of the diet included but little, if any, sodium chloride

The average daily insensible loss for the 19 day period was 1,402 Gm (Chart 15)

The average insensible loss per day in the series ranged from 1,154 Gm to 1,830 Gm The average for 175 twenty-four hour periods was 1,457 Gm Of the total output of each case the insensible loss ranged from 30.8 per cent to 49.6 per cent or an average for all cases of 39.4 per cent (Table I)

Benedict and Root⁶ have shown that the insensible loss is approximately proportional to the body weight Levine, *et al*,²⁶ have also shown a similar relationship between insensible loss and body weight, height and surface area The cases considered in this study were arranged in order of their body weight irrespective of the type of the surgical procedure Although the study was

not conducted with the patients at basal conditions, there exists an apparent relationship between the size of the body and the insensible loss

There were two cases which did not follow this relationship. The first, Case F M (Chart 10) was a female, age 22, five feet three inches tall, weighing 161 pounds. She had chronic cholecystitis and cholelithiasis. Her stature and the disease suggest a metabolic disturbance. The daily insensible

TABLE I
SUMMARY OF INSENSIBLE LOSS DETERMINATIONS

Case	Height	Weight in Kilo- grams	Sur Area Sq Meter	Days	Average Daily Insensible Loss		Insensible Loss Per- centage of Total Output	
P P	5' 2 "	47 57	1 45	21		1,180	33 2	
I E	5' ¾"	49 08	1 43	7		1,154	32 4	
E H	5' 1¾"	49 24	1 48	10	Preop	1,889	47 2	
				6	Postop	1,244	37 0	
					Ave	1,647	44 0	
E B	5' 3¾"	50 95	1 51	8	Preop	1,467	38 3	
				7	Postop	1,321	28 6	
					Ave	1,399	33 3	
E M	5' 6¼"	56 59	1 64	8		1,341	43 6	
J T	5' 8¼"	57 29	1 67	19		1,402	30 8	
L R	5' 7¾"	61 50	1 73	10		1,503	44 0	
C C	5' 3¾"	63 33	1 67	8	1st op	1,498	40 0	
				14	2nd op	1,665	42 6	
					Ave	1,604	42 0	
W P	5' 11 "	66 47	1 85	7		1,638	38 0	
F M	5' 3⅛"	73 44	1 76	15		1,500	40 2	
L K	5' 8¼"	75 10	1 88	13		1,286	41 0	
H S	5' 10¼"	78 63	1 98	8	1st op	1,804	52 0	
				14	2nd op	1,845	43 5	
					Ave	1,830	49 6	
				175	Days—Average—		1,457 Gm	39 4

loss curve was the most irregular of the series. For the size of the patient the average insensible loss for the period was low. The second, Case L K (Chart 5), although well proportioned, had a thick, flabby panniculus adiposus. He was phlegmatic in type and extremely inactive both mentally and physically. For the size of the patient the average insensible loss for the period was extremely low.

It is interesting to note that the hyperthyroid cases, after surgical correction of the metabolic disturbance, fell into the proper relationship according to the size of the patient. Prior to operation the insensible loss of these cases was abnormally high.

Discussion —The amount of fluids ordered for a surgical patient is usually determined by the appearance of the patient and the amount of intake and output recorded on the chart for the previous day or days. Respectful attention is always given to the urinary output for the preceding 24 hours before the fluid program is outlined for the day.

The following case illustrates graphically the inadequacy of such a program and the clinical importance of other than perceptible losses.

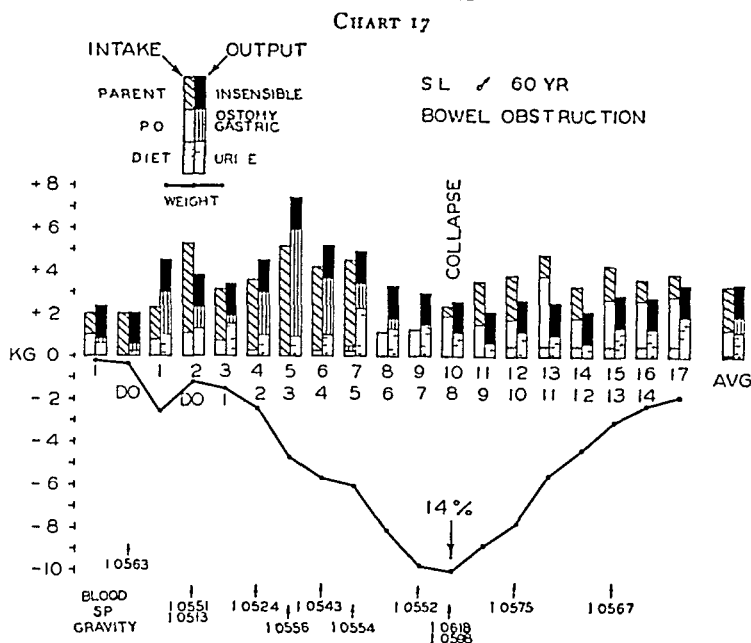
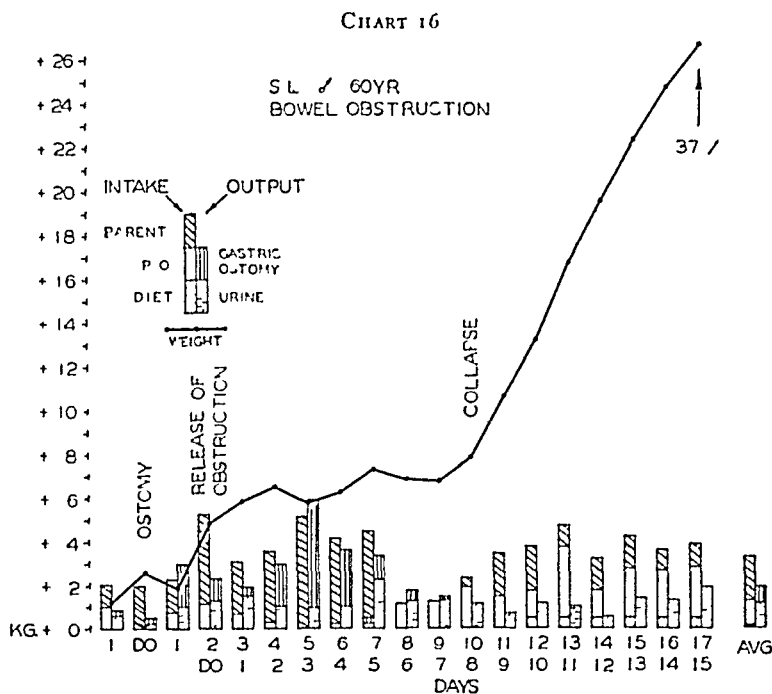
Case S L —(P H No 448691) Enterostomy, Exploratory Celiotomy, Release of Peritoneal Band. The figures which were accepted as a daily guide for fluid administration were taken from the chart and plotted. The difference between the daily intake and output was represented as a cumulative increase or decrease in weight. The cumulative gain of intake over output amounted to 26.7 Kg, or 37 per cent of the total weight of the patient. It is improbable that the patient retained fluids amounting to 59 pounds for there was an obvious decrease in the weight of the patient during his illness (Charts 16 and 17).

In Chart 17 it will be noted that the intake and the output are the same as in Chart 16, except that to each daily output was added an estimated loss of 1,500 Gm per day. The daily output then exceeded the intake and the curve of the cumulative difference decreased constantly to a point which was 14 per cent below the original weight of the patient. At this point the patient suddenly went into a state of collapse, the extremities became cold, cyanosis was marked, the blood pressure fell, the pulse was rapid and thready and the temperature and respirations increased rapidly. The patient was placed in an oxygen tent and an infusion administered until a transfusion could be given. As a result of this treatment the patient slowly responded and the convalescence thereafter was slow and uneventful. Throughout the remaining postoperative course intake exceeded output, and the weight curve slowly returned toward the normal.

This case demonstrates three important facts, namely, The empiric administration of fluids to be unsatisfactory, the false security of a urinary output which seems to be adequate, and the clinical importance of the insensible loss. It is felt that the collapse of the patient was due to severe dehydration. Eight hours after collapse, and after the above emergency measures were instituted, the specific gravity of the blood was still as high as 1.0618. What the specific gravity was when the collapse occurred is unknown. Collier and Maddock²⁷ have demonstrated, in humans, that after 6 per cent of the body weight in fluids has been lost the subject is on the verge of serious dehydration. Usually urinary output diminishes with progressive dehydration, as demonstrated by Case P P (Chart 14) and Case J T (Chart 15). In Case S L (Chart 17) the urinary output was more than a liter per day. This was considered adequate and parenteral fluids were stopped on the eighth postoperative day. The reserve supply of fluid which was already diminished continued to fall more rapidly, during the next two days, to a maximum loss of 14 per cent. The body was then so depleted of fluid that severe hemoconcentration and collapse occurred.

As previously pointed out, in this series of cases, 39.4 per cent of the total output was lost through the insensible route. This is sufficient to make the insensible loss as serious a dehydrating factor as the urinary output, as demonstrated in Case S L (Charts 16 and 17). Intake exceeded output by far until allowance was made for the insensible loss, at which time a marked

negative balance occurred. It is to be remembered that the dissipation of heat through the vaporization of water continues constantly until the water supply is depleted and a critical state of dehydration exists.



CHARTS 16 and 17—Case S. L. (P. H. No. 448691) Enterostomy, exploratory celiotomy, release of peritoneal band

From a surgical point of view the most common form of deranged water exchange is that of dehydration. The nature of some surgical procedures necessitates a method of therapy which contraindicates the administration of fluid by the usual routes. Frequently this deprivation extends over a period of several days and sometimes a week or longer. Occasionally, persistent vomiting, prolonged enterostomy drainage or forced duodenal drainage is

required which also depletes the body of fluid and electrolytes. Unless fluid is adequately administered by other routes, a state of dehydration is inevitable.

The patients undergoing less extensive surgical procedures are usually capable of maintaining a satisfactory balance of water and salt. The cases in which major procedures are undertaken, especially those on the gastrointestinal tract or those which disturb the normal function of the tract, are dependent upon the judgment of the surgeon for fluid, electrolytes and nourishment.

If dehydration is to be avoided rather than combated, adequate provision must be made to cover these losses, including that lost insensibly. It is impractical to determine the insensible loss of each surgical patient but a reasonable amount, as demonstrated in this study, can be estimated from the size and weight of the patient. Only by recognizing the clinical importance of the insensible loss can replacement be made according to the physiologic requirements of the surgical patient.

SUMMARY

(1) The insensible loss in 12 surgical patients having 14 operations ranged from 1,154 to 1,830 Gm per day.

(2) The average insensible loss for 175 twenty-four hour periods was 1,457 Gm per period.

(3) The insensible loss for all the cases averaged 39.4 per cent of the total output.

(4) The insensible loss varied with the size of the patient rather than with the type or the extent of the surgical procedure.

The authors wish to thank Margaret E. Cordes, R.N., Louise M. Cronin, R.N., and Gladys E. Post, R.N., for assistance with the patients, Edith McMillan, B.A., B.Sc., for assistance with the diets and Dr. John Scudder for technical studies.

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EXCISION OF THE AXILLARY VEIN IN THE RADICAL OPERATION FOR CARCINOMA OF THE BREAST*

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THIS communication presents an argument in favor of the excision of the axillary vein during so-called radical breast operations when involved lymph nodes lie in close or immediate proximity to the vein. The question of indications for or contraindications to radical mastectomy for carcinoma will not be considered, the present discussion being concerned solely with the management of the axillary vein when the radical operation is contemplated. It is quite generally agreed that in the effort to remove the fat and the lymph nodes completely during the customary dissection of the axilla, the axillary vein must be more or less bared and stripped clean. The closer the involved nodes lie to the axillary vein, the greater is the necessity of extensively freeing the vein. The latter has been injured occasionally during this dissection and, according to case reports, has been ligated without untoward effect under such circumstances. On the other hand, no reports have been found which dealt with deliberate excision of the axillary vein in order to achieve a more thorough block removal of the axillary contents.

The argument in favor of excision of the axillary vein in selected cases is simple and can be stated briefly. Although extirpation of every cancerous nest by means of a careful axillary dissection is not to be anticipated, an effort is always made to effect a complete removal of the axillary contents. When there is minimal axillary lymph node involvement or when the invaded lymph nodes are not situated near the vein, the standard dissection may meet all requirements. On the other hand, one experiences a sense of inadequacy during such dissections when involved nodes are close to or lie upon the vein. The likelihood or possibility of leaving on the vein small, perhaps microscopic fragments of cancerous tissue is great. Furthermore, cancer cells within or cancerous involvement of lymph channels represent part of the picture of cancerous invasion of the axilla. When the lymphatic network, which has a well-known tendency to encircle the axillary vein, is involved in immediate proximity to the vein (which is very likely to be the case when cancerous lymph nodes are situated close to the vein), removal of such lymphatic tissue by any procedure other than by removal of the axillary vein appears improbable. It may be argued that, under the foregoing circumstances, a radical operation is futile and the addition of a more radical procedure, purposeless. This view may be correct in one case, and false in another, for there is no way at the present time to prognosticate the ultimate outcome of an operation in any

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given case when involved nodes are situated near the axillary vein. Therefore, as long as the possibility of eradication exists, the objective should be the widest possible block removal of visibly invaded tissue. That purpose is not achieved if involved nodes in close proximity to the axillary vein (with or without involved intercommunicating lymphatics) are dissected from the vein, no matter how cleanly the latter may be stripped by a painstaking technique. In order to attempt to achieve complete removal, the objective is more nearly approached by removal of the vein together with the involved nodes and axillary fat in one block. Thus it appears quite as logical to excise the axillary vein in the block removal of cancerous axillary lymph nodes, as to excise, in the generally practiced manner, the internal jugular vein in the block removal of cancerous cervical lymph nodes.

The deterrent factor in a consideration of excision of the axillary vein unquestionably is the fear of interference with the circulation which might ensue. The belief that obstruction of the main venous trunk of an extremity leads to edema is based presumably on the presence of edema in cases of thrombophlebitis in an upper or lower extremity. Little thought appears to have been given to the fact that perivenous lymphangitis usually exists in cases of thrombophlebitis. Furthermore, there can be no doubt that lymphatic blockade produces edema of an extremity. In any event, the idea that the obstruction of a vein inevitably results in edema is incorrect. The writer has shown and reported^{1 2 3} cases of excision of the axillary, femoral, and iliac veins (for suppurative thrombophlebitis), and has demonstrated that edema of the upper or lower limb respectively did not exist before operation and did not occur after operation.

Despite a logical basis for excision of the axillary vein, it was a far cry from a patient desperately ill from a suppurative phlebitis and septicemia, to one with carcinoma of the breast who might not only not be helped but possibly be harmed by such a procedure. For this reason removal of the axillary vein as part of block removal of the axillary contents was performed in the beginning solely in instances of extensive axillary node involvement. When excision of the vein proved harmless in these earlier cases, the procedure was extended to cases of less extensive perivenous lymph node involvement and to cases in which the nodes did not lie in immediate proximity to the vein.

A brief description of the technic of excision of the axillary vein in the block removal of the axillary contents is sufficient, as no unusual operative procedures have been employed. Nothing is added to the risks of the radical operation, indeed, the dissection of the axilla is aided and simplified. As soon as the axilla is entered, the relationship of involved nodes (if any) to the axillary vein is ascertained. If excision of the axillary vein is decided upon, it is exposed at the apex of the axilla and severed between ligatures, it is again severed in its third portion, in the same manner, at the lateral limit of the axilla. The usual dissection of the axillary contents, after severance of the axillary vein, is simplified, naturally, by the elimination of the dissection required for the removal of nodes about the vein. As a result, the duration

of operation is materially shortened. The existence of a double axillary vein may be recognized only after the more superficial vessel has been divided and freed.

Special histologic studies of the removed vein and adjacent tissues have not been carried out. They might have proved conclusively the advantages which I have claimed for the procedure in question. Of course, the pathologic material available from the small number of cases in which excision of the vein has been practiced might also have failed to supply conclusive evidence. There was, however, a significant finding in one specimen removed at operation. Immediately adjacent to the vein was a lymph node which was so minute that it could be seen macroscopically, as a speck, only in the stained section. It is interesting to note that microscopically part of this node was found to be invaded by cancer and part was uninvolved. Whether this node, not visible in the operative field or in the gross specimen, would or would not have been removed by the standard dissection about the axillary vein cannot be stated definitely. One may assume that there was an equal chance that it would have been left behind, particularly because of its intimate relationship to the axillary vein.

Concerning the question of improvement in end-results by the addition of excision of the axillary vein to the customary radical operation, any statement made at this time would be entirely valueless, because the procedure has been employed only in 11 cases. A definite statement can, however, be made concerning the question of edema following operation. Some edema of the upper arm followed the operation in two instances, and there was fluctuating edema of the hand in two other cases. This represents, perhaps, the incidence of edema following the radical operation when the axillary vein is not excised. However, exact figures are of no moment for we are not concerned with statistics. The essential innocuousness of removal of the axillary vein is established even by the small number of cases in which it has been undertaken. As stated at the outset the purpose of this communication was to set forth an argument in favor of excision of the axillary vein when cancerous lymph nodes lie in close or immediate proximity to the vein. The argument appears logical and to that extent warrants the belief that improvement in the end-results might come to pass if the proposed step were added, in selected cases, to the standard dissection of the axilla in the radical operation for cancer of the breast.

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DISCUSSION—DR EMIL GOETSCH (Brooklyn, N Y), apropos of the question of the edema of the arm, following radical resection of the breast, recalled Doctor Halsted speaking of the causes which he thought influenced this condition. He paid particular attention to the wound healing following radical resection and found, after a study of a considerable series of cases, that in instances in which the wound healed without discharge of serum or seropurulent secretion, indicating a mild infection, edema of the arm did not follow, even in instances in which the axillary vein was involved or possibly ligated. In those cases in which there was even the mildest infection, indicated by the discharge of a cloudy serum, edema of the arm was likely to follow. He came to the definite conclusion that the edema was not due to any particular procedure involving the axillary vein but rather to the occlusion by fibrosis of the lymphatics remaining after the resection. This fibrosis is primarily the result of infection and because of it the possibility of subsequent improvement in the edema is remote. Accordingly, Doctor Halsted felt that the condition of the axillary vein is not the determining factor in the case with edema.

DR JOHN E JENNINGS (Brooklyn, N Y) reported his experience with regard to the procedure under discussion, stating that he had accidentally ligated the vein, probably half a dozen times, with resection of the vein in small segments, as part of the attempt to remove all the axillary contents. Only recently, however, had he with "malice," as Doctor Neuhoﬀ described it, removed the vein in very much the way that has been described. Doctor Jennings has done this in six cases within the last three years, two of whom died promptly within three or four days after operation. In one an autopsy was obtained and a clot was found in the subclavian vein, with the rest of the clot, or a considerable portion of it, in the pulmonary artery. In the other case, which was considerably more difficult to do, death occurred in about the same way but no autopsy was obtained. Doctor Jennings felt there is a limited field for this procedure. The exposure of the axilla is better, and its apex can be better cleared of the fascia. There are certain cases where it is almost necessary to do this if one is to accomplish a complete removal of the lymphatics of the axilla after intensive radiation. If one is going to impose radical surgery upon radical radiation one will often find it exceedingly difficult to clear the vein, a complete evidement is only possible by its resection. Eventually the limits of surgery in dealing with cancer of the breast will be found, but a word of caution is not amiss—it is possible to go too far.

DR GEORGE H SEMKEN (New York) The studies of Florence Sabin, Huntington and McClure, and von Schulte have shown the close genetic relationship of the lymphatics and the veins. Sabin showed that the jugular lymph sacs, for example, were formed by the coalescence of small veins at the venous confluence in the neck, which were first emptied of their contained blood, and later, after coalescence, again joined the subclavian or internal jugular veins or both. From these sacs, a centrifugal development of lymph vessels then occurred. Eventually, the sacs became groups of lymph nodes. The other observers demonstrated the existence of primordia in various areas of the mesenchyme, from which angioblasts were developed, which became blood vessels and lymph vessels respectively, and developed centripetally. It is almost axiomatic that the lymphatic trunk vessels tend to accompany the veins of the respective regions.

In the relationship of the lymphatics of the breast to the axillary vein—the axillary vein is not properly comparable to the internal jugular vein. In

the neck (excluding the superficial chain of lymphatics), the submental and submaxillary lymph nodes, which form the first line of defense for their respective drainage areas, are alone distant from the internal jugular vein. The carotid packet of the deep chain, next to these in the lymph stream, is, however, immediately regional to the tongue, fauces and pharynx, epipharynx and the larynx. These nodes lie directly at and upon the internal jugular vein, and from this point downward, the successive nodes in this lymph stream are closely related to the vein. Many of these nodes have efferents directly into the vein. Early fixation of invaded lymph nodes to the vein is, therefore, frequently found in the neck. In the axilla, however, the relations of the mammary lymphatic vessels and node groups to the axillary vein are different. The lymph nodes immediately regional to the breast are the anterior thoracic (or pectoral) group. In these nodes, cancer may remain localized for some time. Next in line are the nodes of the central group. From these, the further course is an arc to the axillary vein and then paralleling it to the infraclavicular node group at the clavicle, to end in the subclavian trunks. Fixation of the nodes to the axillary vein is, therefore, relatively long delayed. This anatomic relationship has been clearly demonstrated by Oelsner, Mor-nard, Poulier, and Most, who injected the breasts of cadavers, mainly of newly born infants. The summarized findings are well shown in the chart of Poirier (reproduced in Gray's Anatomy).

In the usual type-case of mammary cancer that is considered operable, even in the presence of fairly advanced primary tumors and palpable axillary lymph-nodes, it has not been a frequent experience to find cancerous lymph nodes fixed to the axillary vein. There does not seem to be any compelling reason, therefore, to resect the axillary vein routinely in every case. Rather, this resection, partial and not complete, should be reserved for the cases in which there is actual or imminent fixation of the lymph nodes.

The excision of the vein has disadvantages and danger. The obstruction to the venous return is not sufficient to cause much edema, but it delays the early restoration of function in the arm. The danger lies in the possibility of a fatal pulmonary embolism. Embolism is favored by the formation of a large clot in a long, dead pocket in the vein, and a resultant ascending thrombosis, and this is the probable status when the vein segment is excised at the first site of lymph node fixation, in the area of the thoraco-acromial vessels, because of the ligation and section of the upper axillary tributaries in the radical breast operation. This danger is lessened if the upper ligature is placed near the entrance of the small tributary veins at the clavicle, which will leave no noteworthy pocket in which the blood can become stagnant and be clotted. It is desirable, also, to avoid an undue inflammatory reaction about the ligated vein. The vein is, therefore, skeletonized, to minimize the amount of resultant dead tissue in the ligated stump, and a double strand of No. 000 chromic catgut is employed for the ligation, instead of a heavy or nonabsorbable ligature.

When the fixation of cancerous lymph nodes to the axillary vein has necessitated the excision of the related segment of the vein, the microscopic examination of this issue has usually shown that the fixation has been limited to the sheath, without invasion of the vein wall, and this has been the characteristic finding, also, in the secondary operations upon cases recurrent after previously incomplete operations. Evidently then, it is the vein sheath and not the vein that is the site of potential cancer involvement, and this finding seems to make it imperative to remove the accessible parts of the sheath of the axillary and basilic veins with the mobilized tissues, routinely in all pri-

may, radical operations This dissection will include a large part of the deep layer of the sheath, where small lymph nodes may lie

The primary need in the radical breast operation is the complete understanding of the paths of cancer extension, a comprehensive and well ordered plan of operation, and a painstaking anatomic dissection This should emphasize the wide removal of the skin of the breast, especially in the neighborhood of the tumor, an incision adequate to afford full exposure of each part of the proposed field of operation, thin flaps, the complete removal of the pectoralis major and minor muscles, the special care to clear the anterior intercostal spaces, the precise and methodical clearing of the axillary and subscapular spaces, and the complete removal of the areolar tissue over the floor Particularly important is the need of care during the operation, to avoid any pressure upon the tumor and the related tissues, which might loosen cancer plugs and give rise to distant metastases

POSTOPERATIVE ROENTGENOTHERAPY IN CANCER OF THE BREAST*

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IN 1922, the writer,¹ in association with Doctor Peck, and again, personally,² in 1927, published articles upon the results of operation on cancer of the breast in which the surgical procedures employed differed from the classic operations of Halsted³ and Meyer,⁴ in that the pectoralis minor was not removed, the amount of excised skin was less, and skin grafting rarely employed. Toward the latter part of the second period² subcutaneous dissection, as advocated by Sampson Handley,⁵ was more frequently employed. Although our percentage of five-year postoperative freedom from recurrence was comparable to that reported from other clinics, we were subjected to unfavorable criticism on the ground that a proper dissection of the axilla could not be made if the pectoralis minor was allowed to remain in place, and secondly, that our reported local recurrence of 36 per cent was due to the fact that not enough skin had been excised, notwithstanding the employment of the Handley modification. The first criticism was considered valid and subsequently the pectoralis minor was removed with the other tissues en masse, in many instances. It will be noted later that the former procedure has still been employed in many of the cases. It has been felt, however, that with the Handley modification, sufficient skin surrounding the tumor could be removed and still permit closure in all cases except those with small breasts or large tumors.

Surgeons are accustomed to judge the adequacy of their operative procedure by the cure of the disease locally. A recurrence in the operative field has usually been considered a reflection upon the operator. Lewis and Rienhoff,⁶ in March, 1932, reported a study of the results of the radical Halsted operation with immediate Thiersch skin graft. In Table XXIX they give complete data on the first site of recurrence in 225 cases. Of these, 79, or 35 per cent, developed a local recurrence. When the technic was varied, only to the extent of removing less skin to allow plastic closure of the wound, there was a local recurrence in 36 out of 77 cases, or 46.7 per cent.

In this series, we have complete data on 119 patients followed for five years, relative to the first site of recurrence. Of this group, 46, or 38 per cent, had local recurrence. We noted, as of special interest, that the recurrence in the axillary region was confined to the cases in which the pectoralis minor had been left in place. Adverse criticism, in a measure, is

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TABLE I

ANALYSIS OF POSTOPERATIVE RESULTS IN 227 CASES OF
CARCINOMA OF THE BREAST*January 1, 1922—December 31, 1931*

Radical operations	227
Operative deaths	5
Dead intercurrent disease	7
Dead of cancer within five years	123
Alive over five years with recurrence	8
Alive over five years and well	55
Lost (not followed five years)*	29

* Many of the cases lost were favorable cases without metastases, and some had known four-year freedom from recurrence. So that in arriving at a percentage of five-year "cures," the cases lost, and those who died of intercurrent disease have been eliminated. We would then have 55 out of 191 cases, or 27 per cent, alive and well at the end of five years.

probably justifiable if a local recurrence appears. Observation, however, on many cases has convinced the writer that the recurrences in the intercostal spaces near the sternum are the result of retrograde growth from internal mammary nodes that were already involved at the time of the operation. It is also thought that even with the most meticulous and thorough surgery, the incidence of local recurrence without roentgenotherapy will remain around 30 per cent. It has been observed that the cancer is rarely confined to the area of the operative field in instances in which a local recurrence occurs. Indeed, it is not uncommon to find coincident regional or distant metastases.

TABLE II

SITES OF FIRST RECURRENCE IN 119 INSTANCES

Local	46
Other breast	7
Supraclavicular	6
Chest	27
Abdomen	14
Osseous	19
	—
	119

Since 1921, the use of high voltage therapy in the treatment of carcinoma of the breast has received increasing consideration. There are some roentgenologists who are satisfied to rely on roentgenotherapy alone. At the other extreme, there are surgeons who feel that there is no benefit to be derived from roentgenotherapy. The Halsted type of operation had become well established before roentgenotherapy came into vogue, so that we may use the reports from such operations as criteria. Nevertheless, one must bear in mind the variation in the course and character of different breast cancers. Many with no treatment live for years, many with inadequate operation in our group have lived long with no recurrence. On the other

hand, many cases that looked favorable have died within a few months In this type no form of treatment seemed to be of value

TABLE III
ANALYSIS OF FIVE-YEAR RESULTS IN THREE CLINICAL TYPES OF 186
CARCINOMATA OF THE BREAST

(A) No Metastases (Axillary)					
Roentgen Ray		No Roentgen Ray			
R *	P M †	R	P M		
8	7	1	7	Dead	23
13	15	3	10	O K	41
5	0	0	1	Recurrence active	6
—	—	—	—		—
26	22	4	18		70
(B) Metastases Not Palpable (Axillary)					
Roentgen Ray		No Roentgen Ray			
R	P M	R	P M		
12	26	3	5	Dead	46
4	4	1	1	O K	10
1	0	0	1	Recurrence active	2
—	—	—	—		—
17	30	4	7		58
(C) Metastases Palpable (Axillary)					
Roentgen Ray		No Roentgen Ray			
R	P M	R	P M		
16	20	4	14	Dead	54
2	2	0	0	O K	4
0	0	0	0	Recurrence active	0
—	—	—	—		—
18	22	4	14		58
Total roentgen-rayed—No metastases		48	28 O K	= 58%	
No roentgen-ray—No metastases		22	13 O K	= 59%	
Total roentgen-rayed—Metastases		87	12 O K	= 13%	
No roentgen-ray—Metastases		29	2 O K	= 3%	

186

* R = Radical operation
† P M = Pectoralis minor allowed to remain with removal of less skin

Roentgenotherapy alone has been used, so far, on such small groups of cases that no definite final opinion may be expressed

Interstitial radium therapy alone has been employed for some years by Keynes ^{7, 13} Recently he wrote ¹³ "I wish to emphasize again the fact that interstitial radium treatment is strictly comparable with surgical operation, in that it is a local form of treatment For this reason no striking improvement in the survival rate was to be expected if radium was to be used as an alternative to surgery It is the metastases, and not the primary disease, that usually cause the death of the patient, and for that reason I never shared the exaggerated hopes that were one time placed by some people in the future

of radium." He has published¹³ a five-year report on 201 cases. When the disease was confined to the breast, clinically, 71.4 per cent (of 75 cases) were alive at the end of five years. When the disease was confined to the breast and axilla, 29.3 per cent (of 66 cases) were alive at the end of five years. When the disease was advanced or inoperable, 23.6 per cent (of 60 cases) were alive at the end of five years. These results compare favorably with results reported when surgery alone has been employed. Keynes has not been completely satisfied with his results, for of late he has added a simple mastectomy to the procedure. He has set down the following rules: (1) Local removal of the tumor if it is large, or the diagnosis is uncertain, followed by radium. (2) Local removal of the breast if the tumor is very bulky, followed by radium. (3) Never dissect the axilla. (4) Radium by itself may be used, (a) if the tumor is of moderate size and the diagnosis certain, (b) if the patient refuses operation. Our experience with these two methods is so limited that we may not express an opinion.

Irradiation before operation has long been advocated but slowly adopted. Its proponents believe that it will reduce the size of the growth, attenuate or kill the scattered cancer cells that may lie in the periphery, and seal off the lymphatics. Thus the operation will become less dangerous in that there is less chance of traumatic emboli with metastasis, or implantation of cancer cells in the wound. If such irradiation is given thoroughly and sufficiently, several weeks to months will be used up in order: (a) To obtain proper effect, and (b) to allow damaged skin to recover. It is also said to interfere with wound repair. Only a few of our cases have had preoperative roentgenotherapy, and in these wound repair was satisfactory.

Postoperative irradiation has a more enthusiastic following. Many believe that the average duration of life has been lengthened. Hermet,⁸ of the Curie Institute in Paris, in a recent article concludes: "We are obliged to state that the question of radiotherapy in cancer of the breast is still long distant from having reached the state comparable to that of radiotherapy of other neoplastic localization. The competition between surgery alone, radiation alone, or their combination remains open. Much work is still necessary before arrival at definite opinions. But we know already that irradiation in a considerable number of cases has increased the prognosis of life."

Westermarck,⁹ in 1930, reported a series of cases treated in 1921-1923 at the Radiumhemmet. After operation, a series of treatments were given to the operative field and the regional nodes including the internal mammary. For the operative field he used a soft filter of 4 Mm. Al at 50 cm. distance. In the axilla he used 0.5 Mm. Cu plus 1 Mm. Al at 40 cm. distance, each dose $\frac{1}{3}$ to $\frac{1}{4}$ S.E.D. A total of 10 to 14 treatments were given in two to three weeks. Seventy-five cases were treated by this method. The surgery had been performed by 19 different surgeons. Thirty-seven per cent were alive and free from recurrence at the end of five years. Twenty-five per cent of the 75 had local recurrences. Forty-five patients had preoperative roentgenotherapy in addition. The preoperative therapy consisted of two tangential

treatments to the tumor with a filter of 0.5 Mm Cu and 1 Mm Al giving $\frac{1}{3}$ S E D. If axillary nodes were palpable treatment was also given to them. Of the 45 thus treated 50 per cent were alive and free from recurrence at the end of five years, while eight, or 17 per cent, had local recurrences. He concludes "It will be clear, therefore, that a five years healing result occurs at a higher rate and that the recurrences are less frequent after a combined surgical and radiologic treatment than after surgical treatment only. This improvement in results is very much in evidence after the pre- and postoperative radiologic treatment."

Wintz,¹⁰ in 1931, has reported on the employment of roentgenotherapy alone. He had 76 per cent five-year cures in 25 cases of Steinthal Group I, and 46.5 per cent five-year cures in 22 cases of Steinthal Group II. Anschütz and Siemens,¹¹ in 1933, reported equally good results with or without postoperative irradiation in a small series (21) of Steinthal Group I cases. But in the Steinthal Group II, they found, in a large group of cases (292), that postoperative irradiation increased their five-year period of freedom from known recurrence 19.6 per cent.

Webster,¹² in 1936, observes that "The tissue dose which has been advised in the treatment of mammary cancer has varied from 700 to 8,000 R. The upper limit of tissue dose advised for breast cancer has been that of Lee and Pack who advanced the view in 1931 that 12 or 13 erythema doses may be advisable. Their erythema was a minimal or threshold erythema, and their dose was obtained by a combined roentgen and interstitial radium technique." Webster uses 2,000 to 4,000 R for simple fractional roentgenotherapy. He treated 182 cases, three-fourths of whom belonged to the Steinthal Group II, the operations having been performed by many different surgeons, with the inevitable variation in surgical technic. With postoperative irradiation he had 42 per cent alive and free from recurrence at the end of five years.

Sufficient reference has been offered to indicate that conservative roentgenologists have had sufficient experience to confirm their belief in the benefit of postoperative irradiation. It must be borne in mind that these reports, of necessity, are based upon the roentgenotherapy of various periods up to 1930. One must also remember that the present attitude of the roentgenologist is that the therapy of that period is archaic. We are told that the present treatment of three to four weeks of fractional doses with a summation of 7,000 to 8,000 R is the only proper method. To a surgeon, it seems to indicate a lack of faith on the part of the roentgenologists in the results that were obtained five or six years ago. Yet, at that time they were most enthusiastic. It had one unfortunate effect upon many surgeons. It made them content with inadequate surgery. They felt that irradiation would prevent any further trouble.

At present, irradiation is given at the most, to the breast area, and the regional nodes. A few also irradiate the mediastinum. But even if the conclusions of the most enthusiastic roentgenologists are accepted and treatment

is instituted both before and after surgery, or confined solely to irradiation, what are we to do regarding the treatment of cancer that appears elsewhere? It will be noted in Table II that the first site of recurrence was recorded in 119 cases of our series. In over one-half, the recurrence was noted outside of the field of irradiation. Shall we suggest in the future that more fields be irradiated, to include the lungs, the other breast, the vertebrae and pelvis, the abdomen? Such a course presents many serious difficulties. Is it possible or feasible? Or should we rest content with local surgery and roentgenotherapy?

TABLE IV
COMPARISON OF TWO ROOSEVELT HOSPITAL REPORTS
Five-Year Results

	1927 ²	1937
No. operated upon and followed-up	157	191
Operative deaths	5	5
Alive and well	58 (36%)	55 (27%)
No. without axillary metastases	55	70
Alive and well	39 (70%)	41 (58%)
No. with axillary metastases	97	116
Alive and well	19 (19%)	14 (12%)
No. with known site of recurrence	88	119
Local recurrence	32 (36%)	46 (39%)
Cases not followed five years	56	29

In the series herewith reported, roentgenotherapy was given after operation. The treatment, up to 1930, was based upon the skin reaction and was usually given in massive doses in one or two treatments to a portal and lasted for 30 minutes to an hour. A 200 kilovolt machine was used, with 5 M A., at a distance of 50 cm. and a filter of 50 Mm. Cu., and 1 Mm. Al. The skin reaction was a severe erythema. This treatment was repeated in two months and again in six months. In a small percentage this was not completed for various reasons.

CONCLUSIONS

We believe that the Halsted type of operation is indicated, except in the matter of skin removal. We have been content to remove a minimum width of five inches of skin in early cases with small tumors, to be followed by the wide subcutaneous dissection as advocated by Sampson Handley. Except in small breasts, we are usually able to effect a plastic closure of the skin. When the tumor is large, more skin must be removed followed by immediate Thiersch skin graft. Our percentage of local recurrence is high, but no higher than those given in the reports from Johns Hopkins Hospital, where the typical Halsted operation is performed.

In 50 cases with known sites of recurrence, in which the Halsted-Handley operation had been performed, there were no axillary recurrences. In 69 cases with known sites of recurrence, in which the pectoralis minor was allowed to remain, there were six local, axillary recurrences.

Surgery gives a five-year prognosis of freedom from recurrence, that varies with the age of the patient, the type of cancer, and the stage of the disease

In our cases without axillary metastases, roentgenotherapy has not increased the prognosis of five-year freedom from recurrence, although it has given to a small percentage the opportunity to live longer

In our cases with axillary metastases, roentgenotherapy has unquestionably given a 10 per cent increase in the prognosis of five-year freedom from disease

It is true that this report is a disappointment to us, in that our percentage results are not as good as those reported by the writer² in 1927. We had hoped to show improvement with the added routine use of the roentgenotherapy then in vogue. Our only possible explanation may be that our pathologic, diagnostic ability is better, and that our cases are more carefully studied and followed up.

In the hope of improvement, during the past three years, we have changed our method to the fractional dose treatment. With this improved method, it is hoped that the incidence of local recurrence may be reduced, and their appearance delayed. Still a real problem is that of regional and distant metastases that are present at the time of operation, although unrecognized. An encouraging approach to this has been made in the sterilization of the patient. I am inclined to doubt the advisability of treating other endocrine glands.

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DISCUSSION DR HUGH AUCHINCLOSS (New York) said that he did not wish to discuss statistics in these cases as they are usually compiled. When he first began studying cancer of the breast he was convinced that statistics would tell the story. Indeed they might, if the many variants, qualitative and quantitative, of the individual cases could be taken into account. After 25 years, it has become perfectly clear that this has not been done and that with

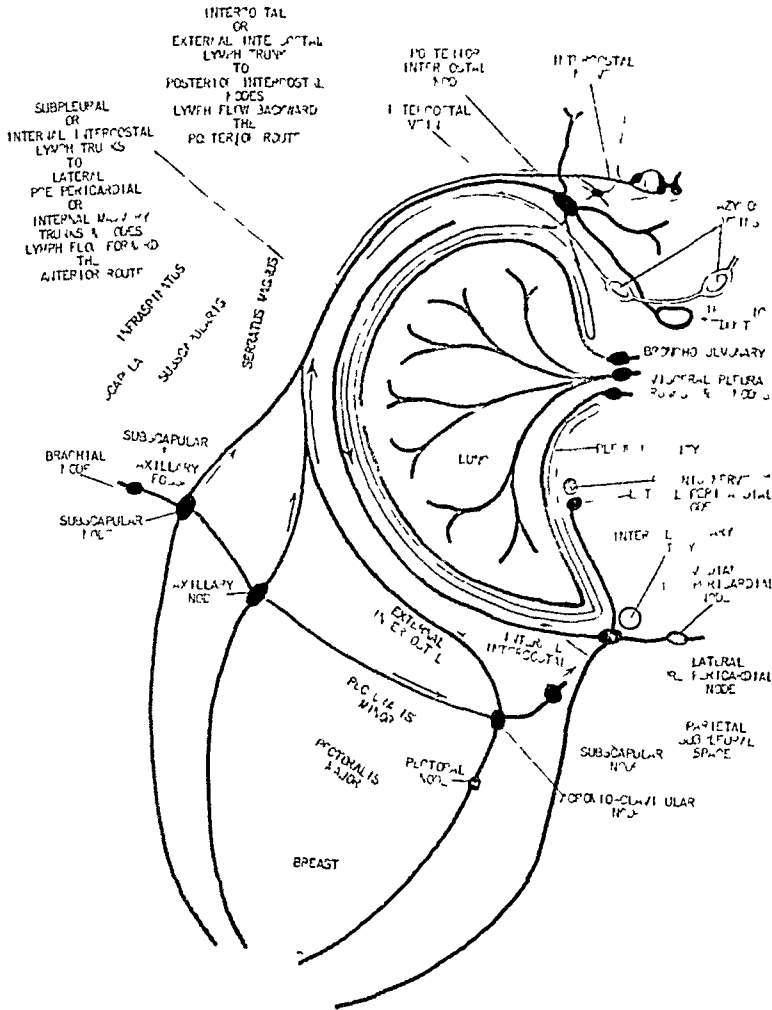


FIG 1.—Diagram to show the lymphatic drainage posteriorly along the intercostal lymph trunks to the posterior intercostal nodes and anteriorly, to the anterior mediastinum where the prepericardial nodes near the internal mammary vessels are situated. The posterior intercostal lymphatics are situated in the so called "zygos route." The anterior mediastinal lymphatics are situated in the subpleural tissues and along the internal mammary vessels phrenic nerve, diaphragm, liver and round ligament. (This drawing is a modification of Fig 10 p 21, from "Cancer of the Breast Clinically Considered" by Cecil H. Lef, one of the most thoughtful treatises on cancer of the breast that has ever been published.)

our present knowledge it is quite impossible. A few of the conclusions drawn from them are truths that have been known for many years. Most of the rest of them are false.

He wished to make it quite clear that he believed he had seen benefits derived from irradiation of breast cancer, but also should like to make it clear that, in spite of these benefits, he had never seen a case proven rid of the disease by the employment of roentgenotherapy alone.

Experienced clinical observers vary widely in their descriptions of the same case. Often one or two microscopic sections, following radiation, have been taken from a place that had been considered typical, yet no cancer was found. If many sections are made from the surrounding areas, however, cancer has always been discovered, or the clinical course has demonstrated that it had not been eradicated.

Hope still exists that irradiation may be made more effective than it is to-day, not only in collaboration with surgery, but that it may even replace surgery. It certainly has not done so as yet, and those who assume that it has, may cause women to lose their lives unnecessarily.

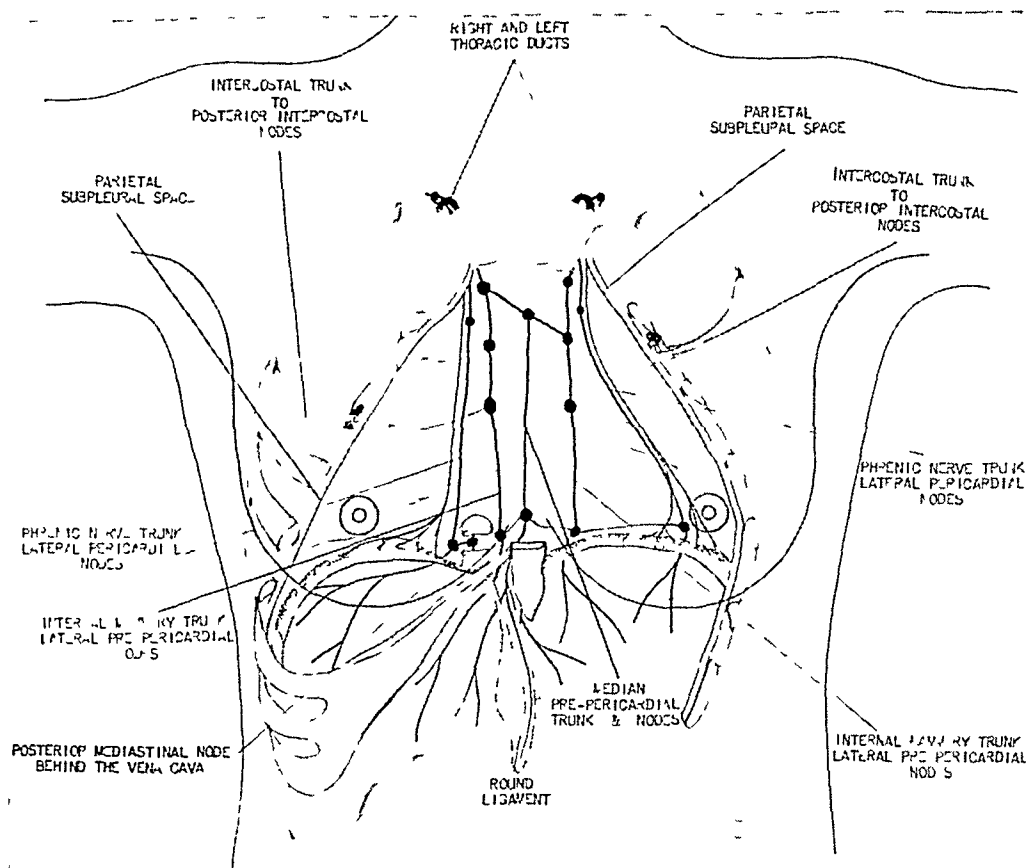


FIG 2—Diagram to show the lymphatic drainage of the inner portion of the breast, the subpleural spaces, the diaphragm, the liver, and the round ligament, to the anterior mediastinal lymph nodes

We must not talk about "axillary node involvement" or "uninvolvement" based upon a clinical examination alone. It is a sure sign of ignorance, if we do. Very large, hard, and even visible masses of nodes have been called metastases, when they were not, and nodes containing cancer have often been overlooked on the physical examination. There is definite proof of this in our records.

One subject has been touched upon that is rather close to our minds and hearts in the study of this disease. Are we irradiating breast cases intelligently? Are we irradiating the tissues that should be irradiated? After all, do we know what tissues to irradiate, for if we do not, what is the use of irradiating at all? If we radiate the breast tumor, or the axilla, we are radiating tissues that, surgically, it has been pretty well demonstrated can be removed successfully. He could think, perhaps, of only one or two cases of "persistences" in the subclavian, axillary and brachial nodes in all the cases that he had personally followed. Occasionally, particularly in advanced cases, there may be a metastasis in the skin in the neighborhood of the excision. But even this

is a relatively rare site for metastases to occur, in our experience. If the skin be widely removed, as Doctor Halsted recommended, and wide undermining,

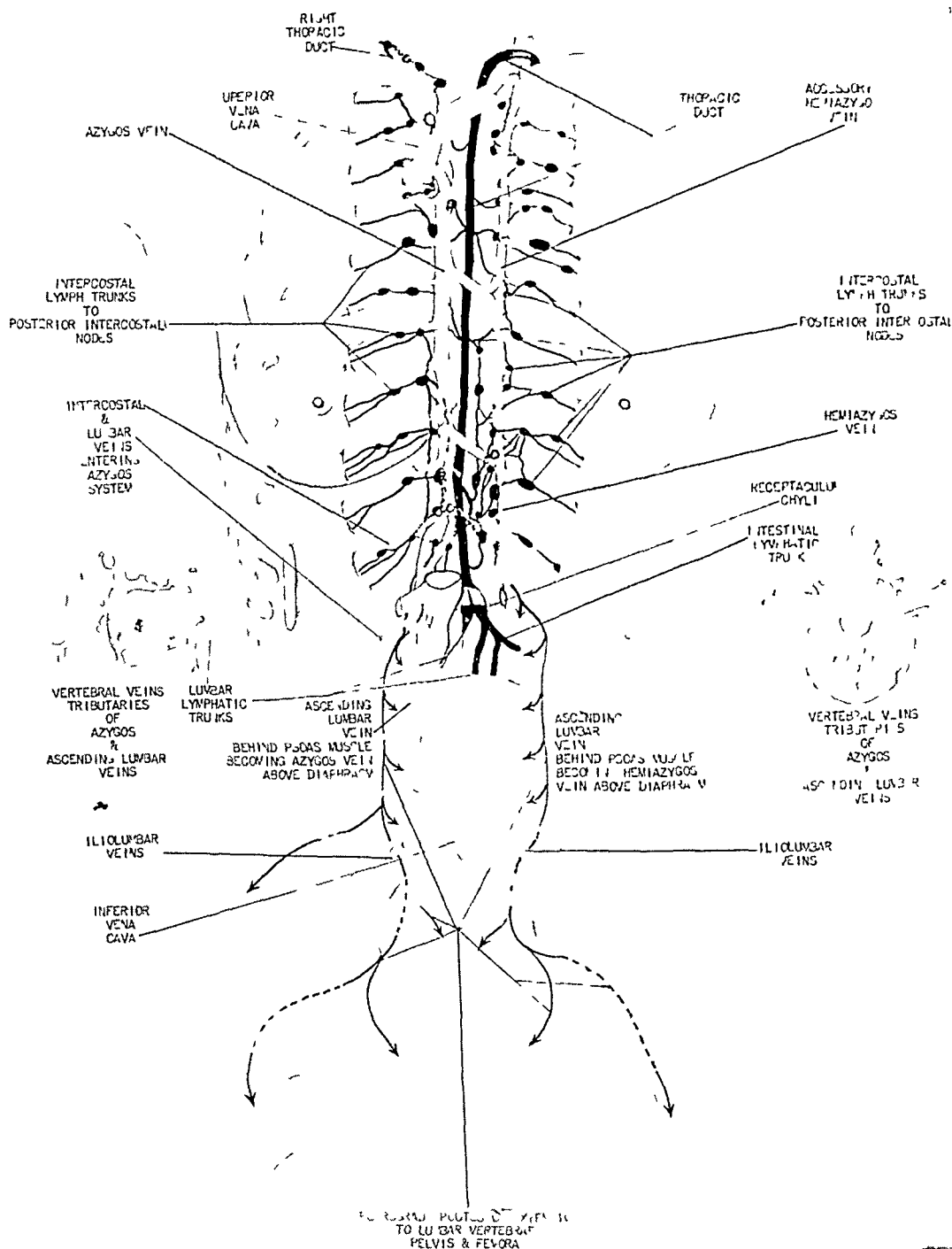


FIG. 3.—Diagram illustrating the so called 'azygos route'. The term "azygos route" is intended for the continuous fascial planes in which are situated the tributaries of the azygos system of veins. In these fascial planes are the lymphatics that drain posteriorly a greater part of the breast. It offers an explanation for the metastases from cancer of the breast to the intercostal spaces, to the posterior mediastinum, to the vertebral bodies to the pelvic bones and retroperitoneal tissues of the pelvis and the femora.

close to the skin, be effected skin metastases are rare. The real trouble lies elsewhere. It lies in those places to which the disease has spread beyond the

tissues capable of being removed by operation. If radiation is to be of value in the treatment of breast cancer, it should be especially directed to those tissues incapable of being removed by operation. These tissues serve as secondary distributing foci.

Most radiation at the present time, indeed practically all of it, is being given to the tissues capable of being removed at operation. It is perfectly true that in doing this certain conducting paths to these quasi "secondary distributing foci" may be radiated. This may be of help, but, if the other secondary distributing foci themselves are not radiated, this effort can be of but little more than temporary value. The important feature of the whole subject, therefore, is to understand where these so-called "secondary distributing foci" exist, so that intelligent radiation may be directed toward them.

The local, so-called recurrences, but better "persistences," of the disease are often thought to be skin persistences when they are not. They are more likely to be persistences of the disease in the intercostal tissues of the anterior or lateral chest wall.

Emphasis has been laid for many years upon the extensions to the so-called supraclavicular lymph nodes. It is true that extensions to the lymphatics above the clavicle occur. As a matter of fact, however, these extensions constitute only a part, and, indeed, rather a lesser part of those extensions that actually cause the death of the patient. The routes along which the disease more often spreads are: To the pleura, anterior mediastinum, vertebral column, liver, pelvic bones, and to the upper portions of the femora, in dramatic contrast to the extraordinarily rare distribution to the lower arms, legs, hands and feet. They are not generally understood. The observations of Sampson Handley and, in particular, those of Cecil H. Leaf, published after his death by Cecil Rowntree in 1912, have been noteworthy contributions on this subject. The accompanying diagrams are offered in the hope that they will present an explanation of the fascial planes that determine, and include, the lymphatic routes along which this disease preeminently spreads to these, above mentioned, tissues.

Extension along the channels indicated in the illustrations presupposes the understanding of dissemination of disease by so-called "circutous" and "retrograde" routes, now generally recognized and accepted by pathologists.

It is hoped that these diagrams may aid in determining more reasonable and logical areas for helpful radiation in breast cancer.

PEPTIC ULCER

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THE present study comprises an analysis of 520 cases of peptic ulcer seen at the Presbyterian Hospital, New York. In each instance the lesion was seen or the diagnosis confirmed by the surgeon or the pathologist. Such a group of so-called "proven ulcers" was examined in detail in order, insofar as possible, to correlate the clinical, pathologic and roentgenologic findings, and to compare these with the observations of other investigators.

It was about a century ago that Cruvelhier (Bevan¹⁰) first distinguished gastric ulcer from carcinoma, and a few years later Quincke (Bevan¹⁶) named the condition "peptic ulcer." Since then an enormous literature has accumulated, attesting to the interest in the subject. Many of the statistics are, however, at variance, due at least in part to the variety of sources drawn upon for information. Thus the pathologist, the roentgenologist, the surgeon and the internist have each approached the subject from a different aspect, often with very little agreement in their results (Albrecht⁷ and Boyd²¹). Variations may be noted from time to time and from place to place, and in the light of more recent knowledge some textbook statistics are subject to question. Robinson,¹²⁵ in an interesting review, has pointed out many of these discrepancies.

Etiology—It is not within the scope of this paper to discuss in detail the many theories advanced to explain the occurrence and chronicity of peptic ulcers. With the exact etiology unknown, certain factors which probably influence the development of such lesions are suggested in the hypotheses offered. It is quite generally felt that the destructive action of the gastric juice brings about a condition which is unique in its chronicity, as well as in its localization in a mucosa which is bathed by such secretions. To this latter fact the presence of peptic ulcers in the esophagus, Meckel's diverticulum and at the site of a gastro-enterostomy is offered as evidence, inasmuch as ectopic gastric mucosa has been frequently found in these situations when so involved (Lindau and Wulff,⁹³ and Matthews and Dragstedt¹⁰⁰). Gastric hyperacidity or the failure of regurgitation of alkaline duodenal secretions to reduce gastric acidity have been advanced as the primary initiating factor by many, including Sippy,¹³⁶ Bolton,²⁰ Boyd,²¹ Chace,²⁸ Deaver and Burden,⁴⁰ Dragstedt,⁴⁵ Hurst and Stewart,⁷⁶ Karsner,⁸² Martin and Burdin,⁹⁸ Matthews,⁹⁹ Mann,⁹⁷ Miller,¹⁰³ Morton,¹⁰⁶ Moszkowicz,¹⁰⁷ Osler,¹¹¹ Robinson,¹²⁶ Somervell and Orr,¹³⁹ and Rivers.¹²¹

Deficiencies of blood supply and vascular "accidents" have been discussed as etiologic factors by many others (Bevan,¹⁶ Eggeis,⁴⁶ Wilbur in Euster-

man and Balfour,⁵² Friedenwald and Love,⁵⁷ Gaither,⁵⁹ Hauser,⁶⁸ Karsner,⁸² Mayo,¹⁰¹ Miller,¹⁰³ Osler,¹¹¹ Payr,¹¹⁴ Reeves,¹¹⁸ Robinson,¹²⁵ Smithies,¹³⁷ Somervell and Orr,¹³⁹ Vitchow,¹⁴⁹ and Wilkie¹⁵³)

The presence of ulcers in nervous, so-called dynamic individuals and particularly in association with periods of stress, fatigue and emotional tension, has been described with increasing frequency in recent writings. In this connection Robinson's¹²⁵ article is of interest. Among the large group who have expressed views on this subject are Bevan,¹⁶ Blahd,¹⁸ Brown in Cecil,²⁷ Chace,²⁸ Wilbur in Eusterman and Balfour,⁵² Hunt,⁷⁴ Hurst and Stewart,⁷⁶ Kaiser,⁸¹ Osler,¹¹¹ Rivers,¹²¹ Robinson,¹²⁶ Smithies,¹³⁷ and Somervell and Orr.¹³⁹

Interesting indeed is the possibility of the association of the mental state with changes in the gastric vascular bed. An imbalance in the vegetative nervous system has been considered to be an etiologic factor by Beaver and Mann,¹³ Cushing,³⁸ Hartzell,⁶⁶ Singer,¹³⁴ and Von Bergmann,¹⁵⁰ among others.

Some authors concede that trauma may give rise to peptic ulcers, in certain situations, either by direct violence to the abdomen, or as might occur with certain harsh foods or foreign substances in the diet (Robinson,¹²⁵ Brown in Cecil,²⁷ Rivers,¹²¹ Blahd,¹⁸ Boyd,²¹ Osler,¹¹¹ and Somervell and Orr,¹³⁹ Gallagher⁶⁰)

Other etiologic factors which have been suggested include focal infections (Bevan,¹⁶ Brown in Cecil,²⁷ Wilbur in Eusterman and Balfour,⁵² Hunt,⁷⁴ Meisser,¹⁰² Miller,¹⁰³ Osler,¹¹¹ and Robinson¹²⁵), and a local infection such as a gastritis or duodenitis (Boyd,²¹ Wilbur in Eusterman and Balfour,⁵² Konjetzny,⁸⁸ Orator and Metzler,¹¹⁰ Puhl,¹¹⁷ Karsner,⁸² Osler,¹¹¹ Rosenow,¹²⁸ and Smithies¹³⁷). A diffuse inflammation of the stomach or duodenum has been noted to be a frequent precursor of ulcer by Bevan,¹⁶ Blahd,¹⁸ Smithies,¹³⁷ and Wilbur in Eusterman and Balfour.⁵²

Alcohol and tobacco have been seriously considered as a cause of ulceration, but probably have more to do with the maintenance of the condition (Bevan¹⁶ and Hunt⁷⁴). Somervell and Orr¹³⁹ studied a large group of Indian natives and believed a vitamin deficiency to be the inciting agency. Endocrine disturbances are mentioned by Karsner⁸² and Chace.²⁸ Curling,³⁷ in 1842, pointed out the association of ulceration of the duodenum with severe burns. Cushing³⁸ pointed out the association of peptic ulceration with disease, particularly with tumors involving the midbrain. Diseases of the abdominal viscera other than the stomach and duodenum, and particularly the gallbladder and the appendix, have been thought to have some bearing on the subsequent formation of peptic ulcers (Aaron,¹ Braithwaite,²² Hunt,⁷⁴ Osler,¹¹¹ Miller¹⁰³). The presence of aberrant Brunner's glands in the gastric mucosa in association with ulcer was reported by Corria,³⁵ who felt that this might be an etiologic factor.

In summary, it would seem that peptic ulcers arise in an area of mucosa in which the resistance has been lowered by any one or several processes. This area is bathed by gastric juice, which may well increase the smallest injury, and in some manner contribute to the chronicity of the disease.

Frequency and Distribution—Peptic ulcer patients are apparently increasing in number from year to year (Boyd,²¹ Chace,²⁸ Hinton,⁷⁰ and Wilkie¹⁵²) The general population apparently suffers from this malady in percentages which are quite consistently in the values of 15.20 per cent (Brown in Cecil,²⁷ Osler,¹¹¹ and Sturdevant and Shapiro¹⁴⁶) Somevill and Orr,¹³⁹ in India, estimated the frequency to be much lower (0.5 per cent), indicating the variability associated with different places of study Hurst and Stewart⁷⁶ considered as many as 10 per cent of the population to be sufferers

In hospital admissions the frequency is in about the same ratio (11.18 per cent) (Emery and Monroe,¹⁸ Goldman,⁶⁴ Lynch⁹⁴) Table I analyzes the ratio-incidence among 118,878 admissions to the Presbyterian Hospital, New York, in the years 1924-1934, inclusive Of these, 1,829 were for peptic ulcer, or about 1.5 per cent These ulcer admissions were found to represent 1,460 patients, suggesting the frequency with which such patients make more than one visit for treatment

TABLE I

ANALYSIS OF THE INCIDENCE OF PEPTIC ULCER AMONG GENERAL HOSPITAL ADMISSIONS

(Presbyterian Hospital, 1924-1934, incl)

Total hospital admissions 1924-1934, incl	118,878	
Total admissions for ulcer 1924-1934, incl	1,829	1.5%
Gastric ulcer	464	
Duodenal ulcer	1,365	
Total patients admitted for ulcer 1924-1934, incl	1,460	
Gastric ulcer	384	
Duodenal ulcer	1,076	
Total number of autopsies studied	2,395	
Total cases showing ulcer	174	7.2%
Sex distribution—average for four months (all hospital admissions—about 3,600 patients)		
Males		51.5%
Females		48.5%
Race distribution—average for four months (all hospital admissions—about 3,600 patients)		
White		88%
Black		11.5%
Other		0.5%

In a study of autopsy material the frequency is usually higher Sturdevant and Shapiro¹⁴⁶ noted that 2 per cent of 7,700 postmortem examinations revealed peptic ulcers Cleland,³² in 1,000 consecutive autopsies, found 18 gastric and 11 duodenal ulcers, or a total percentage of 2.9 Hurst and Stewart⁷⁶ report 5.75 per cent, and Bevan¹⁶ quotes the studies of Hart in Berlin who discovered some evidence of ulceration in 10 to 12 per cent of all autopsies Robertson and Hargis¹²⁴ and Stewart¹⁴² give similar statistics In 1,000 autopsies Lehmann⁹² found 20.2 per cent to have either a frank ulcer or a scar Table I shows that among 2,395 consecutive autopsies studied, 174, or 7.2 per cent, showed peptic ulcers

From other sources an even higher incidence is reported For example,

a group of "dyspeptics" yielded 24 per cent positive cases in a series studied by Albrecht.⁵ Suspected cases studied roentgenologically by Kirklin in Eusterman and Balfour⁵² revealed 13.1 per cent to have ulcers, and in a group of similar cases Percy and Beilin¹¹⁵ found 19.2 per cent.

Sex Distribution—In all of the reports studied the predominance of male patients in both the gastric and duodenal ulcer groups is apparent (Boyd,²¹ Moynihan,¹⁰⁹ and Oslei¹¹¹). In those summaries which group all cases as "peptic ulcers," the ratio of males to females varies from 11.10 to 48.10 (Blackford and Dwyer,¹⁷ Brown in Cecil,²⁷ DeLario,⁴¹ Eusterman and Balfour,⁵² Lynch,⁹⁴ Smithies,¹³⁸ Stewart¹⁴² and Wilkie¹⁵²). In gastric ulcer patients, most authors find the predominance of men less marked than in the duodenal group (Chang,²⁹ Cleland,³² Emery and Monroe,⁴⁸ Jordan,⁷⁹ Lynch,⁹⁴ Percy and Beilin,¹¹⁵ Roof¹²⁷ and Wilkie¹⁵²). Quite in contrast, however, are the reports of Hinton and Trabek,⁶⁹ who found the ratio to be 7.7:10 for gastric ulcers, and of Miller, Pendergrass and Andrews,¹⁰⁴ whose ratio in this group was 6.6:10.

Table II shows the sex distribution and type of ulcers in the series, and indicates that the ratios of males to females were about the average of the above cited reports. The ratio for all of the cases is 3.6:1, 3.7:1 in the gastric, and 3.5:1 in the duodenal cases. Little variation is noted between the medical pathology, surgical pathology and celiotomy cases. A four month survey of all admissions to the Presbyterian Hospital showed the distribution of the sexes to be essentially equal (Table I).

Racial Distribution—Table II shows the racial distribution in this group of patients, which when compared with the four month survey of admissions, as indicated in Table I, would seem to show no racial selectivity. Many reports show a tendency for the white race to be more frequently the victim of peptic ulcer (DeLario,⁴¹ Lynch⁹⁴ and Roof¹²⁷). Robinson¹²⁶ quoted many figures from different parts of the world to support his conclusion that peptic ulcer is "found only among susceptible individuals of the white race."

Age Incidence—The age of the patients is analyzed in Table II, with the youngest and the oldest in each classification. These statistics would seem to indicate that gastric ulcer patients were slightly older than those with duodenal ulcer (49.5 and 44 years, respectively). This is in accord with the conclusions of Blackford and Dwyer,¹⁷ Eusterman and Balfour,⁵² Hunt,⁷⁴ Miller, Pendergrass and Andrews,¹⁰⁴ Percy and Beilin¹¹⁵ and Roof¹²⁷. The average age in each type of ulcer corresponds closely to that given as most frequent by the majority of writers (Blackford and Dwyer,¹⁷ Boyd,²¹ Chang,²⁹ Cleland,³² DeLario,⁴¹ Emery and Monroe,⁴⁸ Eusterman and Balfour,⁵² Hinton and Trabek,⁶⁹ Hunt,⁷⁴ Jordan,⁷⁹ Lynch,⁹⁴ Miller, Pendergrass and Andrews,¹⁰⁴ Oslei,¹¹¹ Percy and Beilin,¹¹⁵ Robertson and Hargis,¹²⁴ Roof¹²⁷ and Smithies¹³⁸). Percy and Beilin¹¹⁵ give 69 as the age of their oldest gastric ulcer patient and 15 as that of the youngest. Of their duodenal cases, the oldest and youngest were 74 and 18, respectively.

Location—In allocating ulcers to the stomach or to the duodenum the

TABLE II
ANALYSIS OF TYPES OF ULCER, SEX AND RACIAL DISTRIBUTION, AND AGE INCIDENCE

	—Medical Pathology—			—Surgical Pathology—			—Celiotomy—			—Totals—		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
Total patients	76	79	19	44	60	11	38	180	13	158	319	43
Total ulcers	95	98	19	55	71	11	51	193	13	201	362	43
Male	77 (81%)	78 (80%)		40 (73%)	47 (66%)		41 (80%)	156 (81%)		158 (79%)	281 (78%)	
Female	18 (19%)	20 (20%)		15 (27%)	24 (34%)		10 (20%)	37 (19%)		43 (21%)	81 (22%)	
White	84 (88%)	90 (92%)		50 (91%)	69 (97%)		46 (90%)	176 (91%)		180 (89%)	335 (92%)	
Black	9 (10%)	5 (5%)		4 (7%)	1 (1%)		3 (6%)	11 (6%)		16 (8%)	17 (5%)	
Yellow	2 (2%)	3 (3%)		1 (2%)	1 (1%)		2 (4%)	6 (3%)		5 (3%)	10 (3%)	
Average age at au- topsy or admis- sion	53.6 yrs	50.8 yrs		47.2 yrs	43.6 yrs		44.2 yrs	40.8 yrs		49.5 yrs	44.0 yrs	
Youngest	18	4		23	12		23	20		18	4	
Oldest	76	83		78	67		72	68		78	83	

marked predominance of the latter site is seen in all but the postmortem series (Table II). A review of the literature shows the ratio of duodenal ulcers to gastric ulcers to vary from 111 to 951 for clinical reports (Albrecht,⁵ Balfour,⁹ Blackford and Dwyer,¹⁷ DeLario,⁴¹ Hinton and Triabek,⁶⁹ Eggleston,⁴⁷ Emery and Monroe,⁴⁸ Hinton,⁷⁰ Holmes and Schatzki,⁷³ Hurst and Stewart,⁷⁶ Lynch,⁹⁴ Miller, Pendergrass and Andrews,¹⁰⁴ Osler,¹¹¹ Percy and Beilin,¹¹⁵ Roof,¹²⁷ Smithies,¹³⁸ Sutherland,¹⁴⁷ Walton¹⁵¹ and Wilkie¹⁵³). In the series herewith reported the ratio of duodenal to gastric ulcers is about 21. In contrast, Boyd²¹ states that gastric ulcers are probably more frequent than duodenal, and several reports obtained from an analysis of pathologic material would tend to agree (Cleland,³² Eusterman and Balfour,⁵² Lehmann,⁹² Robertson and Hargis,¹²⁴ and Sturdevant and Shapiro¹⁴⁶). However, Stewart,¹⁴² reporting postmortem findings found duodenal to exceed gastric ulcers. The possibility arises that the inclusion of acute ulcers by the pathologist may be an explanation for this discrepancy. In this series such ulcers appear almost exclusively in the autopsied group (Table III), and are more frequent in the stomach than in the duodenum. It may be that some of these are of the type of "erosions" described, among others, by Steinberg¹⁴¹.

Combined ulcers, that is, ulcers in both the stomach and duodenum in the same patient, were present in 8 per cent of the cases. This is higher than in the report by Albrecht,⁵ with a frequency of 17 per cent, by Emery and Monroe,⁴⁸ with 18 per cent, or in those by DeLario⁴¹ and Sturdevant and Shapiro,¹⁴⁶ with 3 per cent each. Kirklin in Eusterman and Balfour⁵² found 15 per cent of gastric ulcers to be associated with duodenal ulcers and 6 per cent of duodenal ulcers to be associated with gastric ulcers. Carman²⁵ concurs with the former figure and Walton¹⁵¹ with the latter. Wilkie's¹⁵² 51 combined ulcers in 362 peptic ulcer patients would indicate a frequency of 15 per cent. Rivers¹²² found a coexistence of 13 per cent.

Pathology—Pathologically, gastric and duodenal ulcers may be considered together, as the lesions are essentially similar. Each occurs in a portion of the digestive tract which has much in common with the other, both embryologically and anatomically. The stomach and duodenal bulb arise from the foregut, both have blood supply from the celiac axis, and each is bathed by acid gastric secretion (Boyd²¹). The majority of peptic ulcers are located in the gastric "*magenstasse*" and the bulb, and here the vascularity has the common characteristic of an "end-artery type," with a paucity of capillaries (Bevan,¹⁶ Reeves,¹¹⁸ Wilkie¹⁵³).

By far the greatest number of benign gastric ulcers are seen in a limited area of the lesser curvature. As shown in Table III, 77 per cent of the gastric ulcers were situated on the lesser curvature in the area of the "*magenstasse*" (gastric pathway). The anterior wall of the stomach was the next most frequent site. Sproull,^{140a} in 1931, analyzed all of the reported cases of gastric ulcer occurring on the greater curvature of the stomach, and concluded that benign ulcers in this site are extremely rare. In the Presbyterian Hospital series this was also found to be the case. Two and one-half per

cent of the gastric ulcers were found to be on the greater curvature. This represents four cases, all of which were "acute ulcers" noted at postmortem. Not a single instance of chronic, benign ulcer of the greater curvature was found. Welch (Osler¹¹¹) reported the lesser curvature to be only slightly more frequently involved than the posterior wall. This is at variance with the usual opinion of other observers, which agrees more closely with the results indicated in this series (Bevan,¹⁶ Boyd,²¹ Eusterman and Balfour,⁵² Holmes and Hampton,⁷² Karsner,⁸² Kohler,⁸⁷ Miller, Pendergrass and Andrews,¹⁰⁴ Rivers,¹²¹ Roof¹²⁷ and Stewart¹⁴³).

In actual contact with the pylorus, or definitely involving it in the process of the disease, there were 13 per cent of the gastric ulcers in the cases here reported. DeLaino⁴¹ found 4 per cent at this site, but in most series the only statement is "near the pylorus," making comparisons with this finding difficult. The farthest from the pylorus of any gastric lesion was found to be 18 cm., as measured on the specimen resected at operation, while the average distance for this group was 3.9 cm. This is the region just distal to the incisura, and is the site of predilection noted by most authors (Boyd,²¹ Chang,²⁹ Eusterman and Balfour,⁵² Hinton and Tiabek,⁶⁹ Holmes and Schatzki,⁷³ Karsner,⁸² Moynihan,¹⁰⁹ Stewart,¹⁴³ Sturdevant and Shapiro¹⁴⁶).

The average size of the craters of benign gastric ulcers is most frequently stated to be "under 3 cm." Alvarez⁶ considers such ulcers rarely to exceed 2.4 cm., and Boyd²¹ places the usual upper limit at 2 cm. Chang²⁹ found 70 per cent of 63 cases to be under 3 cm. in diameter, the smallest measuring but 6 mm. and the largest, 5 cm. MacCarty in Eusterman and Balfour⁵² reports benign ulcer craters varying in size from 1 mm. to 19 cm., while Robertson in Eusterman and Balfour⁵² places the average size of the crater at 1 cm. Sturdevant and Shapiro¹⁴⁶ analyzed 120 cases and recorded an average of 2.35 cm. The average, noted in Table III, for this group is 1.66 cm. with the smallest being considered a healed or microscopic crater and the largest 8 cm. across.

Duodenal ulcers are practically limited to the bulb, very few being noted beyond this portion. Only one of the 287 studied in this series was beyond the distal bulb, it being found in the third portion. Of the remaining cases the most distant was five centimeters, and the average measurement, from the proximal margin, of the entire group was 0.79 cm. Only 11.5 per cent of the cases were in actual contact with the pyloric ring. These findings are consistent with the general opinion of others. Boyd²¹ and Kohler⁸⁷ place 90 per cent of ulcer craters within the first one and one-half inches of the duodenum. Roof¹²⁷ found 73.5 per cent less than 2.5 cm. beyond the pylorus. Jefferson⁷⁸ reported that 99.2 per cent of 496 duodenal ulcers were above the ampulla of Vater. In the Presbyterian Hospital series (Table III) about 70 per cent of the duodenal ulcers were on the anterior wall, the remainder being distributed about equally on the posterior and the superior surfaces. Only a small number were on the greater curvature or inferior side. Kohler⁸⁷ does

TABLE III

ANALYSIS OF THE LOCATION, SIZE, TYPES, AND RESULTANT DEFORMITY OF ULCERS IN 447 PATIENTS

Location	Medical Pathology			Surgical Pathology			Celiotomy			Totals		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
No of cases giving locus	66	56		53	67		41	104		160	287	
Ant wall	14 (21%)†	18 (32%)*		18 (34%)*	41 (61%)*		20 (49%)*	140 (85%)*		52 (32%)*	199 (69%)*	
Post wall	5 (8%)	29 (52%)		12 (23%)	24 (36%)		6 (15%)	16 (10%)		23 (14%)	69 (24%)	
Less curvat	60 (91%)	23 (41%)		41 (77%)	15 (22%)		22 (54%)	28 (17%)		123 (77%)	66 (23%)	
Gr curvat	4 (6%)	5 (9%)		0 (0%)	1 (2%)		0 (0%)	4 (3%)		4 (2½%)	10 (3%)	
Av distance to pylorus	5.3 cm	9.8 cm		3.8 cm	5.8 cm		2.1 cm	8.2 cm		3.7 cm	7.9 cm	
Farthest from pylorus	12.0 cm	5.0 cm		18.0 cm	3.0 cm		16.0 cm	4.0 (1 in 3rd portion)		15.0 cm	5.0 cm	
Involving pylorus	10 (10%)†	2 (2%)†	6 (33%)†	8 (15%)†	10 (14%)†	5 (45%)†	8 (16%)†	20 (10%)†	8 (61%)†	26 (13%)†	42 (12%)†	19 (11%)†
Size												
Av size crater	1.73 cm	1.3 cm		1.6 cm	.8 cm					1.66 cm	1.05 cm	
Largest crater	7.0 cm	5.0 cm		8.0 cm	4.0 cm					8.0 cm	5.0 cm	
Types												
Acute	46 (48%)†	33 (33%)†		0 (0%)†	0 (0%)†		1 (2%)†	2 (1%)†		47 (23%)†	35 (10%)†	
Chronic	36 (38%)	57 (58%)		48 (87%)	59 (83%)		43 (85%)	179 (96%)		127 (63%)	295 (81%)	
Hc. uld	4 (4%)	8 (8%)		2 (4%)	11 (15%)		4 (8%)	12 (6%)		10 (5%)	31 (9%)	
Carcinoma in old ulcer	9 (9%)	0 (0%)		4 (8%)	1 (2%)		3 (6%)	0 (0%)		16 (8%)	1 (0.3%)	
Scarring												
No of cases noting scarring	94	88		55	68		45	179		194	335	
None	50 (53%)*	32 (36%)*		0 (0%)*	0 (0%)*		1 (2%)*	2 (1%)*		51 (26%)*	34 (10%)*	
Slight—no deformity	1 (1%)	11 (13%)		3 (5%)	1 (2%)		8 (18%)	23 (13%)		12 (6%)	35 (10%)	
Marked—no deformity	8 (8.5%)	17 (19%)		6 (11%)	15 (22%)		7 (15%)	30 (17%)		21 (11%)	62 (19%)	
Slight—with deformity	7 (7.5%)	2 (2%)		3 (5%)	11 (16%)		7 (15%)	41 (23%)		17 (9%)	54 (16%)	
Marked—with deformity	28 (30%)	26 (30%)		43 (79%)	41 (60%)		22 (50%)	83 (46%)		93 (48%)	150 (45%)	

* Percentage of those giving this data

† Percentage of all ulcers

not agree with this, placing the greater portion on the superior aspect of the bulb Karsner⁸² believes the posterior wall is more often involved

The crater of a duodenal ulcer is usually smaller than that of a gastric lesion, averaging about 1 cm in this series Craters were noted as varying from a minute, microscopic ulceration to one with a diameter of 5 cm Deaver,³⁹ MacCarty in Eusterman and Balfour,⁵² and Studevant and Shapiro,¹⁴⁶ all place their cases within this same range

Table II also indicates the well-known fact that peptic ulcers are frequently multiple There were 201 gastric ulcers in 158 patients and 362 duodenal ulcers in 319 patients

As might be expected, the "combined" ulcers more frequently involved the pylorus (Table III), inasmuch as many lay on both the duodenal and gastric side of the muscular ring and were continuous over its surface

The microscopic picture in peptic ulcer is variable They may be acute, chronic or healed, and in this series the chronic type was most frequently found The acute ulcers were more frequent in the gastric group and the healed more numerous in the duodenum (Table III) This has been commented upon above as offering a possible explanation for the lack of agreement of the pathologic and clinical statistics No comparable reports were found in the literature

The ulcer crater may be represented by a small, shallow erosion, or penetrate the wall to varying depths, or perforate to an adjacent viscus or into the peritoneal cavity They are most frequently deep and callous, involving the submucosa and muscularis (Caiman,²⁵ MacCarty in Eusterman and Balfour,⁵² Boyd²¹) The margins of the crater may be overhanging, receding or terraced (Boyd,²¹ MacCarty in Eusterman and Balfour,⁵² Osler,¹¹¹ Robinson¹²⁵) In the specimens observed in this series, the overhanging margin was seen to predominate The lumen of the crater is usually filled with mucus and debris Beneath this is a rather typical layering or stratification From within outwards there is first seen a level of necrotic granulation tissue, then a zone of healthy granulations with numerous young capillaries, and finally dense scar tissue The latter varies greatly in amount and in extent, with the resultant deformity in the adjacent tissues showing marked differences In general, some distortion is present in all cases showing scarring, and scarring is noted in the greater proportion of all ulcers, except in the acute type Disturbance in structure due to fibrosis (Table III) was more marked in the gastric group than in the duodenal, but the differences were not significant Severe degrees of distortion are exemplified by the permanent hour-glass contraction of the stomach and by the shortening which may occur in the pyloropapillary distance in the duodenum The normal for this distance is given as 8 cm, and it may be reduced to 3 to 4 cm by contracting fibrous tissue (Robertson in Eusterman and Balfour⁵²)

Varying with the age and the activity of the process, the cellular reaction may be of different types and degree Polymorphonuclear neutrophils are seen in the earlier, more active lesions, while lymphocytes and plasma cells

predominate in those of longer duration (Boyd²¹) Vascular changes of the nature of peri-arteritis and endarteritis have been reported, and thrombosed vessels may be seen (Boyd,²¹ Dible⁴⁴)

The mucosa about the crater is often distorted by scar tissue and bizarre formations may result due to regeneration and proliferation The down-growing epithelium may be pinched off by fibrocytes, leaving packets of epithelium to be seen in the section The muscularis mucosa may be fragmented or hypertrophied (Steinberg¹⁴¹) Edema, to a greater or lesser degree, is apparent in the adjacent submucosa

Complications and Mortality—A discussion of the mortality in peptic ulcer is essentially that of the complications of the disease Patients do not die of peptic ulcer *per se*, but of hemorrhage, perforation, carcinomatous change, obstructive phenomena or the operative procedures undertaken to correct these or to relieve severe symptoms

Hemorrhage is so common that it may be regarded as a symptom, according to Karsner⁸² It occurs when an ulcer, acute or chronic, involves a vessel as the necrotizing process extends (Boyd,²¹ Karsner⁸²) Bleeding may be slight or massive, and the latter is sometimes fatal Protective thrombi may be dislodged by peristalsis, distention or an increase in systemic blood pressure (Karsner⁸²) Hemorrhage, according to Barclay,¹² is unrelated to the ulcer's size, site, or even presence Others, including Goldman⁶⁴ and Boyd,²¹ consider bleeding to be more frequent in posterior wall duodenal ulcers and lesser curvature gastric ulcers The gastroduodenal artery and its source, the superior pancreaticoduodenal artery, are involved in duodenal ulcers, and the coronary (gastric) arteries in gastric ulcers (Goldman⁶⁴) The involved arteries may be held open as a result of the stiffening of their walls by fibrous tissue (Robertson in Eusterman and Balfour⁵²) Rivers in Eusterman and Balfour⁵² expresses the view that duodenal ulcer is the most frequent of all causes of gastro-intestinal bleeding, and that 90.5 per cent of such ulcers bleed at some time Table IV shows melena and hematemesis to be equally prevalent in this series, and that gastric and duodenal ulcer patients suffer these complications in about equal proportions although somewhat less perhaps than those with combined lesions In general, slightly more than one-third of the patients bled to some degree, a figure that is in accord with that of several others (Balfour,¹¹ Emery and Monroe,⁴⁸ Goldman,⁶⁴ Hurst and Ryle,⁷⁵ Osler,¹¹¹ MacGuire,⁹⁵ Lynch,⁹⁴ and Paterson¹¹³) Smithies¹³⁸ recorded a frequency of 36.4 per cent of hemorrhage, with hematemesis occurring in 81 per cent of these and melena in the remaining 19 per cent This predominance of hematemesis over melena is in contrast to the findings of Chace²⁸ and of Brown in Cecil,²⁷ who express the opinion that melena occurs in about 25 per cent of ulcer patients and hematemesis in less than 10 per cent Gaither⁵⁹ and Eggleston,⁴⁷ as well as Hurst and Stewart,⁷⁶ place the frequency at 18 to 19 per cent As noted above, there was no difference between the percentages of bleeding ulcers in the gastric or duodenal groups in this series Some authors have not found this to be true, notably

Blackford and Dwyer,¹⁷ who found massive hemorrhage to be twice as frequent in the stomach (30 per cent) as in the duodenum (15 per cent) Crohn³⁶ is in agreement with the increased tendency of gastric ulcers to bleed in comparison with those in the duodenum, as are de la Viesca,⁴² Percy and Beilm,¹¹⁵ and Eusterman and Balfour.⁵² Roof,¹²⁷ however, feels that duodenal ulcers bleed more frequently than gastric

Again it is here apparent that a difference in the source of the cases studied may account for the variation in the impressions gained by the writer. For example, Hurst and Stewart⁷⁶ agree with the statistics of Crohn³⁶ who places the frequency of hemorrhage at 20 per cent for hospital cases and 10 per cent for all cases of peptic ulcer. This seems to be a fairly reasonable estimate. It is of interest that Somervell and Ori,¹³⁹ in their group of cases in India, found hemorrhage exceedingly rare.

Perforation (Table IV) occurred with equal frequency in gastric and duodenal ulcers. Goldman,⁶⁴ in a large number of cases, obtained a percentage exactly in accord with the finding in the series herewith reported, namely, 23 per cent. This figure is somewhat higher than that of Miller, Pendergrass and Andrews,¹⁰⁴ who found 15 per cent in their series of operated cases. Roof¹²⁷ found that ruptured ulcers made up 18 per cent of his gastric and 20.4 per cent of his duodenal cases. Among other investigators the usual figures are around 5 to 10 per cent (Blackford and Dwyer,¹⁷ DeLario,⁴¹ Emery and Monroe,⁴⁸ Lynch⁹⁴). These figures vary in different localities, as do so many statistics. Somervell and Ori,¹³⁹ from India, report only four perforations in 2,500 operatively proven ulcer patients.

The average age in patients with perforated ulcers is somewhat lower than that for the group as a whole. Judin,⁸⁰ Sallick,¹²⁹ and Miller, Pendergrass and Andrews¹⁰⁴ are in agreement as to this fact. Perforation is more frequent in ulcers of short duration, often with histories of no more than a few days or weeks (Boyd²¹). This was most striking in the present series, in which a surprising number had an acute episode, associated with rupture and resultant peritoneal irritation, as the presenting symptom of ulcer. Emery and Monroe,⁴⁸ among others, have commented upon this dramatic onset. Patients with histories suggesting the presence of fibrotic, chronic ulcers seldom perforate with symptoms of peritonitis. More often penetration gradually occurs into the adjacent viscera, particularly the liver and pancreas (Boyd²¹).

The controversial subject of the origin of carcinoma in previously benign gastric ulcers is met with frequently in the extensive literature on peptic ulcer. Using the criteria of Chang²⁹ and others, which criteria include a history of sufficiently long duration (at least two years, and a previous roentgenologic diagnosis of ulcer if possible), location of the lesion in the region of greatest frequency for benign ulcers, and the presence of malignant changes only on one margin and not in the base of the crater, a percentage of 8 was found in gastric ulcers (Table III). This figure is admittedly open to question, as no two observers might interpret the same material in the same

manner (Scott,^{132, 133} Spilsbury¹⁴⁰) It is the belief of Hinton and Trabek⁶⁹ that carcinoma never arises in benign ulceration and Morley¹⁰⁵ considers it exceedingly rare Sauer¹³⁰ felt that such a process occurred in but one of 182 gastric ulcer cases The most frequent figure appearing in the literature on the subject is about 5 to 6 per cent or less (Balfour,¹⁰ Boyd,²¹ Cabot and Adie,²³ Brown in Cecil,²⁷ Chang,²⁹ Dible,⁴⁴ Emery and Monroe⁴⁸ Ewing,⁵³ Huist and Stewart⁷⁶) Osler¹¹¹ indicates a 5 to 10 per cent possibility, and Stewart¹⁴³ found evidence of carcinoma in 14 of 216 cases at autopsy, or at operation Roof¹²⁷ and Walton¹⁵¹ gave 10 per cent as the incidence, while Eusterman and Balfour⁵² found malignant changes in 10 to 15 per cent of resected gastric ulcers Thus it is apparent that there is no definite agreement, and that the problem is not an easy one either clinically or pathologically Bloomfield¹⁹ divides gastric carcinomata into two main groups—those which arise in stomachs showing chronic gastritis and anacidity, and those with ulcer Landon⁹⁰ is convinced that carcinoma is a sufficiently frequent follower of gastric ulcer to cause concern

It will be noted in Table II that one case of carcinoma following duodenal ulcer is recorded In this instance, a long standing, callous ulcer of the duodenum was found in contact with a carcinoma of the stomach, one lying on either side of the pyloric ring The association, of course, cannot be proven Carcinomata originating in duodenal ulcers must be exceedingly rare, as is malignant disease of the duodenum Jefferson,⁷⁸ in analyzing all of the reported cases of duodenal carcinoma, found only 31 apparently having their origin in preexisting duodenal ulcer

The mortality and causes of death found in this study are shown in Table IV These figures cannot be considered as a fair statistical average, for being hospital cases they represent the relatively more severe Death due to ulcer was highest in the combined and gastric groups, being almost twice as frequent as in the duodenal Perforation accounted for the most deaths in the combined ulcer group, carcinoma in the gastric and operative procedures in the duodenal The latter figure is to be anticipated when the large number of operative cases reported in this series is considered The total operative mortality is, however, extremely low in this duodenal group, namely, 87 per cent, even though this was most frequently the cause of death Death occurred in a somewhat later age period than that in which the patients were first seen Death due to carcinoma arising in ulcer was about at the same average age as that for the ulcer group as a whole

Goldman⁶⁴ found the mortality in a group of 890 patients to be 17 per cent Of those with perforation 32 per cent died, a figure above that obtained in this series (14 to 16 per cent—not shown on the table) Eleven point one per cent of patients with hemorrhage died in this group, which agrees with the Presbyterian Hospital figures (10 per cent of duodenal and 15 per cent of gastric ulcers) Blackford and Dwyer¹⁷ report a mortality of eight in 207 duodenal ulcer cases, a percentage of 3.9 Of these, two deaths were due to hemorrhage, and three each succumbed following operation and perforation

DeLaino's⁴¹ series of 105 peptic ulcers showed death due to ulcer in only two cases, both of which were postoperative. Emery and Monroe⁴⁸ showed a death rate of 7.2 per cent, and of those cases with perforation, 28 per cent ended fatally. Hunt,⁷¹ in a recent report, estimates that the mortality in peptic ulcer is somewhere around 2 to 5 per cent, which, in view of the marked variation in the statistics of other authors, would seem to be a fair average. Postoperative deaths are probably more frequent than deaths due to other causes associated with ulcers, but such a statement should be qualified by calling attention again to the fact that surgical cases are those which have done poorly under conservative treatment or those which are suffering from severe complications.

Before leaving the subject of the complications of peptic ulcer, mention should be made of the disturbed or altered physiology of the involved viscus. Spasm, deformity, delay in emptying, variations in peristalsis, changes in tonus and hypersecretion are all demonstrable roentgenologically. A discussion of these phenomena, therefore, will be considered in that section.

Much has been written about the relationship of ulcers to disease of the gallbladder and appendix. This association was studied only in the celiotomy group (Table IV). It is difficult to believe that this relationship is significant as here found. A history of an appendectomy is not always evidence of appendicitis, nor is one of "gallbladder trouble" a diagnostic certainty. Sufficient information was not found on the charts to make this a reliable estimate. A causal relationship between the appendix and peptic ulcer has been previously mentioned. Aaron¹ was impressed by the physiologic relationship of these structures and noted that pressure on the appendix caused pyloric spasm and epigastric pain. In groups where this problem has been carefully analyzed the frequency of an association is often recorded as higher. Alvarez⁷ found gallbladder disease in 85 per cent of male gastric ulcer patients and in 13.3 per cent of female patients. In the duodenal ulcer patients 11 per cent of the men and 27 per cent of the women had associated disease of the gallbladder. Rivers and Mason¹²³ found 13 per cent of their operated duodenal ulcers to have definite cholecystitis pathologically, and in another 33 per cent the findings were suggestive. Their gastric cases showed 7.8 per cent of probable gallbladder disease. Emery and Monroe⁴⁸ reported associated gallbladder disease in 13 per cent of their ulcer cases, and Smithies¹³⁸ 14 per cent. In 18 cases of gastric ulcer at postmortem, Cleland³² found gallstones in three. From the other side the statistics are less impressive. Hartman and Rivers⁶⁵ found ulcer in 3.2 per cent of 879 cases of cholecystitis, which is not much above the usual frequency of the disease as an entity. Laird's⁸⁹ percentage of 4.1 led him to believe that the relationship was not direct but slight. As a whole the recorded findings suggest that this is true.

A possible relationship between appendiceal disease and peptic ulcer has not been proved (Emery and Monroe⁴⁸). Hartman and Rivers⁶⁵ reported chronic appendicitis to be present in 35.7 per cent of gastric and 44.4 per cent of duodenal ulcer patients. Smithies'¹³⁸ rate was 36 per cent and Lari-

TABLE IV
ANALYSIS OF COMPLICATIONS AND MORTALITY

	Medical Pathology			Surgical Pathology			Cholecotomy			Totals		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
Complications												
Hemorrhage												
Hematemesis	13 (39%)†	20 (49%)†	4 (36%)†	17 (39%)†	19 (33%)†	4 (36%)†	10 (27%)†	55 (31%)†	5 (38.5%)†	40 (35%)†	94 (34%)†	13 (37%)
Melena	18 (55%)	30 (75%)	6 (54%)	16 (36%)	26 (46%)	5 (45%)	7 (19%)	50 (29%)	5 (38.5%)	41 (36%)	106 (39%)	16 (46%)
Perforation	11 (15%)§	21 (26%)§		5 (9%)§	10 (16%)§		22 (43%)§	30 (22%)§		38 (24%)§	70 (22%)§	
Av age at perforation	49 yrs	48.2 yrs		39.4 yrs	36.3 yrs		35.3 yrs	37.6 yrs		39.8 yrs	40.5 yrs	
Operations												
No. of cases operated upon	18 (24%)§	24 (30%)§	9 (47%)§	44 (100%)§	60 (100%)§	11 (100%)§	38 (100%)§	180 (100%)§	13 (100%)§	100 (63%)§	264 (85%)§	33 (77%)§
History of appendicectomy							5 (12%)§	11 (9%)§				
History of gallbladder disease							1 (3%)§	12 (6%)§				
Mortality												
Death due to ulcer	25 (34%)*	27 (35%)*	10 (59%)*	9 (20%)†	4 (7%)*	2 (18%)*	8 (21%)*	9 (5%)*	1 (8%)*	42 (27%)†	40 (13%)*	13 (30%)*
Hemorrhage	5 (20%)†	8 (30%)†	0 (0%)†	0 (0%)†	0 (0%)†	0 (0%)†	0 (0%)†	0 (0%)†	0 (0%)†	5 (12%)†	8 (20%)†	0 (0%)†
Perforation	3 (12%)	6 (22%)	5 (50%)	0 (0%)	0 (0%)	2 (100%)	3 (37%)	3 (33%)	0 (0%)	6 (14%)	9 (23%)	7 (54%)
Postoperative	8 (32%)	13 (48%)	5 (50%)	5 (55%)	4 (100%)	0 (0%)	2 (26%)	6 (67%)	1 (100%)	15 (36%)	23 (57%)	6 (46%)
Carcinoma	9 (36%)	0 (0%)	0 (0%)	4 (45%)	0 (0%)	0 (0%)	3 (37%)	0 (0%)	0 (0%)	16 (38%)	0 (0%)	0 (0%)
Av age with death due to ulcer	53.2 yrs	52.3 yrs		56.4 yrs	52.2 yrs		54 yrs	49.9 yrs		54.3 yrs	51.7 yrs	
Av age with death due to carcinoma in old ulcer	53 yrs			61 yrs	57 yrs		56 yrs			55.5 yrs	57 yrs	
* Percentage of all ulcers												
† Percentage of cases with death due to ulcer												
‡ Percentage of patients, having complete records (Table VI)												
§ Percentage of ulcer patients												

* Percentage of all ulcers
† Percentage of cases with death due to ulcer
‡ Percentage of patients having complete records (Table VI)
§ Percentage of ulcer patients

more⁹¹ noted that 18 per cent of his cases had had appendicectomies Somervell and Oll,¹³⁹ in statistics from India, found a 73 per cent concomitance

Symptomatology—That the symptomatology and history of peptic ulcer are characteristically those of periodicity, persistence and variable regularity, is almost axiomatic (Osler,¹¹¹ Brown in Cecil,²⁷ Hunt,⁷⁴ Emery and Monroe,⁴⁸ etc) Ulcer patients usually have long histories, Hunt,⁷⁴ noting that it was usually two years before the patients presented themselves to a physician The average duration of symptoms in Emery and Monroe's series⁴⁸ was seven years, and Roof's¹²⁷ was 6.5 years for duodenal and 5.5 years for gastric ulcer patients More than half of Smithies'¹³⁸ cases, and there were 500 gastric ulcers, had had symptoms for from 5 to 20 years Chang²⁹ placed 33 per cent of his gastric cases in this category The average duration of symptoms in our own series was 7.8 years for gastric and 7.3 years for duodenal ulcers This is closely in line with the above findings (Table V)

The periodicity of symptoms is emphasized by the ratios noted in Table V They were intermittent rather than constant, six times as frequently in the gastric and 24 times as frequently in the duodenal cases Remissions occurred in 61 per cent of gastric ulcer patients and 64 per cent of duodenal ulcers in the summary by Miller, Pendergrass and Andrews¹⁰¹ Smithies'¹³⁸ found this phenomenon characterizing 69 percent of his cases, and Roof¹²⁷ commented on the history of "attacks" in 81.2 per cent of duodenal and 78.5 per cent of gastric ulcers The occurrence of exacerbations in the spring and fall has been remarked frequently (DeLario⁴¹) It was Smithies'¹³⁷ belief that the explanation was to be found in the prevalence of "epidemic infectious agents" at these times Eusterman and Balfour⁷² found this seasonal variation in 50 per cent of their series They offered no satisfactory explanation but suggested, in agreement with Smithies, that there might be an increased infectious activity, or possibly that some nutritional factor entered into the question at these times Huist and Stewart⁷⁶ state that the return of symptoms may "definitely date from a sudden change in the weather", "The effect of weather is not entirely direct, it depends in part on the increased liability to nasal catarrh, tonsillitis, bronchitis, and 'influenzal attacks' in bad weather " It is their belief that this seasonal change is much less marked in gastric than in duodenal ulcer patients

Pain is the most constant and important symptom of peptic ulcer The frequency and characterization of the pain in the present series of cases is noted in Table V The descriptive adjectives used are those employed by Miller, Pendergrass and Andrews¹⁰⁴ The percentages of 72, 88 and 83 respectively for gastric, duodenal and combined ulcer patients indicate the very general occurrence of this symptom Hinton⁷⁰ recorded it in almost the exact proportion, 79 per cent Other illustrative statistics include those of Lynch,⁹⁴ with pain present in 69 per cent of gastric and 73 per cent of duodenal cases, Percy and Berlin,¹¹⁵ with 100 per cent of gastric and 92.4 per cent of duodenal cases, and Smithies'¹³⁸ who noted pain in 98 per cent of his gastric ulcers

TABLE V

ANALYSIS OF SYMPTOMATOLOGY

Symptoms	Medical Pathology			Surgical Pathology			Celiotomy			Totals		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
Average duration	8 5 yrs	7 3 yrs		8 3 yrs	7 9 yrs		6 3 yrs	7 0 yrs		7 8 yrs	7 3 yrs	
Intermittent	14	25	5	37	52	10	29	164	10	80	241	25
Constant	2	1	0	6	2	1	6	7	2	14	10	3
Ratio	7 1	25 1	5 0	6 1	26 1	10 1	5 1	23 1	5 1	6 1	24 1	8 1
Pain												
Present	33 (45%)*	37 (52%)*	11 (61%)*	41 (95%)*	56 (95%)*	11 (100%)*	36 (97%)*	175 (98%)*	12 (100%)*	110 (72%)*	264 (88%)*	34 (83%)*
Vague or absent	40 (55%)†	34 (48%)	7 (39%)	2 (5%)	3 (5%)	0 (0%)	1 (3%)	4 (2%)	0 (0%)	43 (28%)	41 (12%)	7 (17%)
Type												
Severe	4 (12%)†	10 (27%)†	1 (9%)†	20 (49%)†	22 (40%)†	5 (45%)†	17 (47%)†	37 (21%)†	2 (17%)†	41 (37%)†	69 (26%)†	8 (24%)†
Dull	4 (12%)	6 (16%)	5 (45%)	6 (15%)	13 (23%)	1 (9%)	5 (14%)	48 (27%)	4 (34%)	15 (14%)	67 (25%)	10 (29%)
Sharp	2 (6%)	3 (8%)	1 (9%)	5 (12%)	7 (13%)	3 (27%)	3 (9%)	32 (18%)	1 (8%)	10 (9%)	42 (16%)	5 (15%)
Gnawing	5 (15%)	6 (16%)	5 (45%)	4 (10%)	10 (18%)	0 (0%)	7 (19%)	22 (13%)	1 (8%)	16 (15%)	38 (14%)	6 (17%)
Cutting	3 (9%)	3 (8%)	0 (0%)	5 (12%)	2 (4%)	1 (9%)	2 (6%)	5 (3%)	1 (8%)	10 (9%)	10 (4%)	2 (6%)
Burning	5 (15%)	1 (3%)	2 (18%)	6 (15%)	11 (20%)	3 (27%)	10 (22%)	26 (15%)	2 (17%)	21 (19%)	38 (14%)	7 (21%)
Aching	0 (0%)	0 (0%)	0 (0%)	2 (5%)	2 (4%)	0 (0%)	0 (0%)	6 (3%)	0 (0%)	2 (2%)	8 (3%)	0 (0%)
Colicky	3 (9%)	8 (21%)	0 (0%)	10 (25%)	4 (8%)	1 (9%)	3 (9%)	29 (17%)	1 (8%)	16 (15%)	41 (15%)	2 (6%)
Tulness or heaviness	6 (18%)	6 (16%)	2 (18%)	14 (34%)	18 (32%)	2 (18%)	13 (36%)	70 (40%)	5 (42%)	33 (30%)	94 (36%)	9 (26%)
Not stated	2 (6%)	8 (21%)	1 (9%)	1 (2%)	0 (0%)	0 (0%)	1 (3%)	1 (0 5%)	1 (8%)	4 (4%)	9 (3%)	2 (6%)
Location												
Epigastric	33 (100%)†	30 (81%)†	10 (90%)†	41 (100%)†	51 (91%)†	11 (100%)†	33 (92%)†	165 (94%)†	11 (92%)†	107 (98%)†	246 (93%)†	32 (94%)†
Rt hypochond	2 (6%)	4 (11%)	3 (27%)	3 (7%)	6 (11%)	2 (18%)	2 (6%)	8 (5%)	0 (0%)	7 (6%)	18 (7%)	5 (15%)
Lt hypochond	3 (9%)	0 (0%)	0 (0%)	6 (15%)	3 (5%)	0 (0%)	2 (6%)	3 (2%)	0 (0%)	11 (10%)	6 (2%)	0 (0%)
Lwr abdomen	2 (6%)	4 (11%)	0 (0%)	1 (2%)	1 (2%)	0 (0%)	4 (11%)	8 (5%)	1 (8%)	7 (6%)	13 (5%)	1 (3%)
Ref to back	5 (15%)	8 (21%)	3 (27%)	11 (27%)	4 (8%)	3 (27%)	0 (0%)	20 (11%)	0 (0%)	16 (15%)	32 (12%)	6 (17%)
Ref to shoulder	0 (0%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0 5%)	0 (0%)
Chest	0 (0%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (6%)	1 (0 5%)	0 (0%)	2 (2%)	2 (1%)	0 (0%)
Relation to meals												
None	3 (9%)†	7 (19%)†	4 (36%)†	2 (5%)†	13 (23%)	† 3 (27%)†	6 (16%)†	24 (14%)†	4 (34%)†	11 (10%)†	44 (17%)†	11 (32%)†
2 hrs or more after	11 (33%)	15 (40%)	2 (18%)	14 (34%)	18 (32%)	2 (18%)	5 (14%)	81 (46%)	2 (17%)	30 (27%)	114 (43%)	6 (17%)
1 5-2 hrs	2 (6%)	0 (0%)	1 (9%)	2 (5%)	3 (5%)	1 (9%)	6 (16%)	13 (7%)	5 (42%)	10 (9%)	16 (6%)	7 (21%)
1-1 5 hrs	3 (9%)	3 (8%)	1 (9%)	6 (15%)	9 (16%)	2 (18%)	4 (11%)	6 (3%)	0 (0%)	13 (12%)	18 (7%)	3 (9%)
5-1 hr	6 (18%)	2 (5%)	2 (18%)	13 (32%)	6 (11%)	2 (18%)	11 (28%)	16 (9%)	0 (0%)	30 (27%)	24 (9%)	4 (12%)
“After”	2 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	1 (3%)	12 (7%)	0 (0%)	3 (3%)	12 (4%)	1 (3%)
“Before”	1 (3%)	3 (8%)	0 (0%)	2 (5%)	3 (5%)	0 (0%)	1 (3%)	10 (5%)	0 (0%)	4 (4%)	16 (6%)	0 (0%)

* Percentage of all cases
† Percentage of patients having pain
‡ Many acute, without symptoms

The type of pain, however, does not seem to denote the site of the lesion. Severe pain was somewhat more frequent in gastric ulcers. "Dull" and "sharp" were both employed more in the duodenal group. "Cutting" and "burning" were a little more usual in gastric than duodenal ulcers. In the combined group "dull" and "burning" were more frequently employed than in other types of ulcers. The general facts in this descriptive analysis agree with those of Miller, Pendergrass and Andrews¹⁰¹. "Sharp, burning" pain was more frequent in their series. Only a small percentage was noted by them to complain of fulness or heaviness, while it will be noted in Table V that approximately one-third of the cases reported such distress. Other reviewers have recorded about the same variations in the intensity of the discomfort (Percy and Beilin,¹¹⁵ Roof¹²⁷). Emery and Monroe¹⁸ described slight distress in 20 per cent of their cases, moderate in 58 per cent and intense in 18.4 per cent. Of their 539 patients with abdominal distress, 136 applied such adjectives as "boiling," "grinding," "gnawing," *etc*, and about one-half complained of fulness.

The allocation of pain to a portion of the abdomen is noted in Table V. It is seen to be predominantly epigastric, as is generally recognized. Four hundred sixty-one of Emery and Monroe's¹⁸ 556 cases were so located. Percy and Beilin,¹¹⁵ Chace,²⁸ Miller, Pendergrass and Andrews,¹⁰⁴ Smithies,¹³⁸ Hunt,⁷⁴ and Roof¹²⁷ have reported this same finding. As might be expected, pain in the right and left hypochondria was more frequent in duodenal and gastric ulcers respectively. Referred pain to the back was present in 15 per cent, with no particular difference in the three types of ulcer. The findings of Miller, Pendergrass and Andrews¹⁰⁴ were similar and somewhat higher than those of Roof,¹²⁷ who found this phenomenon more frequent in gastric ulcers, attributing its occurrence to posterior adhesions. Hunt⁷⁴ ascribes it, especially, to the presence of adhesions to the pancreas, with pain referred to the cardiac and splenic areas as being associated with lesions higher on the lesser curvature. In this connection the analysis of Rivers¹²⁰ is of interest. He reported that pain is poorly localized in 90 per cent of shallow gastric lesions, but definitely placed in 50 per cent of large and 90 per cent of perforating ulcers. In the latter type, where the ulcer involved the mesentery or adjacent viscera, 93 per cent had pain referred to the back or thorax. In duodenal ulcer he found diffuse distress an accompaniment of obstructing lesions. In this region 64 per cent of cases, where the ulcer was not perforating, gave a poorly defined pain distribution, while accurately localizable pain was noted in extensive and subacute ulceration with considerable regularity. In 90 per cent of perforating duodenal ulcers the pain was in the right upper quadrant, and 77 per cent of these remarked that it was also referred to the liver and the back.

The relationship of pain to the time of eating is variable, but it is apparent, from Table V, that pain occurs somewhat earlier in gastric than in duodenal ulcer, and that there is usually some definite relationship. That there is an association is the impression of Miller, Pendergrass and Andrews,¹⁰⁴

Smithies,¹³⁸ Chace,²⁸ and Emery and Monroe⁴⁸ and others Hurst and Stewart,⁷⁶ Roof¹²⁷ and Eusterman and Balfour,⁵² among others, noted that pain was present earlier after eating in gastric than in duodenal ulcers. Eusterman and Balfour,⁵² Smithies,¹³⁸ and Hurst and Stewart⁷⁶ state that pain occurred earlier in gastric ulcers situated in the cardia than in those farther down in the stomach, appearing as early as one-half hour after eating. Hunt⁷⁴ suggested that the nearer the pylorus the ulcer is, the longer the interval between eating and the onset of pain. The regularity of the occurrence of pain, emphasized by Moynihan,¹⁰⁸ did not seem to be frequent or accurate enough to be considered characteristic. Rivers¹²⁰ makes the interesting observation that a change in the characteristics of ulcer pain, with increased persistence, despite the use of alkali, denotes a change in the pathology.

The cause of pain in peptic ulcers has not been definitely determined. An increased acidity with resultant irritation of bared nerve fibrils has been suggested, and Palmer¹¹² produced pain in 95 per cent of tested cases of ulcer by its application. Against this as a universal explanation, is the low acidity in many patients with severe pain (DeLario⁴¹). Even the relief by alkali might be explained by a resultant decrease in muscle spasm, rather than acid neutralization. Spasm, as a cause of pain, has many adherents. Deaver and Burden⁴⁰ and Hurst⁷⁷ considered pyloric spasm as the cause of pain. Barclay¹² described the concurrence of pain, spasm and tension as seen fluoroscopically. DeLario⁴¹ believes that pain occurs only when the base of the ulcer is attached to the muscle of the submucosa or to the muscular coat proper, as by edema, adhesions or inflammatory changes. By such fixation, muscular activity results in tension on the ulcer crater and pain. Brown in Cecil²⁷ agrees with the theory that spasm of the pylorus causes ulcer pain, but adds that neuralgia or neuritis of the gastric nerves may occasionally be responsible. It should be added that many definite ulcers are seen roentgenologically and by direct observation in association with which there has been no pain or discomfort (Boyd²¹).

Table VI shows the number of instances in which case records were adequate for an analysis of other symptoms. Nausea and vomiting were more often encountered in the gastric and combined ulcer groups than in the duodenal, while belching or eructations appear in a larger percentage of the latter. As Miller, Pendergrass and Andrews¹⁰⁴ state, these symptoms are not typical of the disease. The more important symptom, bleeding, has been discussed elsewhere. Constipation is rather frequent, suggesting a close functional relationship between the portions of the gastro-intestinal tract. Anorexia is variable and probably accounts for weight loss, along with food restrictions, vomiting, night pain and lack of sleep (Hurst and Stewart,⁷⁶ Smithies¹³⁸).

Vomiting is associated with pain or with pyloric obstruction, either organic or reflex (Chace,²⁸ Emery and Monroe⁴⁸). As will be discussed later, pyloric obstruction is more frequent in association with gastric ulcers, and

TABLE VI
FURTHER ANALYSIS OF SYMPTOMATOLOGY IN CASES WITH MORE COMPLETE DATA

	Medical Pathology			Surgical Pathology			Ceclectomy			Totals		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
Symptoms												
Nausea	9 (27%)*	11 (27%)	5 (45%)	21 (48%)	39 (69%)	7 (63%)	23 (62%)	83 (47%)	5 (30%)	37 (32%)	133 (49%)	17 (50%)
Vomiting	23 (70%)	34 (83%)	10 (91%)	28 (64%)	39 (69%)	11 (100%)	28 (76%)	123 (70%)	11 (85%)	79 (69%)	196 (72%)	32 (92%)
Erectations	19 (58%)	14 (34%)	6 (54%)	34 (77%)	28 (49%)	6 (54%)	17 (46%)	93 (53%)	4 (31%)	70 (61%)	135 (50%)	16 (46%)
Constipation	16 (48%)	14 (34%)	6 (54%)	25 (57%)	24 (42%)	5 (45%)	15 (41%)	83 (47%)	6 (45%)	56 (49%)	121 (44%)	17 (50%)
Diarrhea	5 (15%)	2 (5%)	1 (9%)	1 (2%)	2 (4%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)	7 (6%)	4 (1%)	1 (3%)
Anorexia	4 (12%)	9 (22%)	3 (27%)	9 (21%)	9 (16%)	1 (9%)	5 (13%)	23 (29%)	2 (15%)	18 (16%)	51 (19%)	6 (17%)
Weight loss	20 (61%)	18 (44%)	9 (81%)	30 (68%)	27 (47%)	4 (36%)	18 (32%)	94 (53%)	8 (61%)	68 (60%)	139 (51%)	21 (60%)
Av loss	20	25	18 75	20	19	18 5	18	15 5	22	20	17	20
Pounds lost per month	2 25	1 25	1 5	1 5	2 5	4	1 3	2 25	1 0	1 7	2 0	2 0
Cases complete enough for study*	33	41	11	44	57	11	37	175	13	114	273	35
Physical Findings												
Local tenderness	16 (50%)	17 (41%)	9 (81%)	29 (66%)	32 (56%)	9 (81%)	31 (84%)	109 (62%)	5 (39%)	76 (67%)	158 (58%)	23 (66%)
Rigidity	2 (6%)	8 (20%)	3 (27%)	4 (9%)	5 (9%)	3 (27%)	15 (41%)	27 (15%)	1 (8%)	21 (18%)	40 (15%)	7 (20%)
Spasm	2 (6%)	9 (22%)	0 (0%)	4 (9%)	5 (9%)	1 (9%)	9 (24%)	33 (19%)	0 (0%)	15 (14%)	47 (17%)	1 (3%)
Visible peristalsis	4 (12%)	2 (5%)	1 (9%)	1 (2%)	2 (4%)	0 (0%)	2 (5%)	9 (5%)	1 (8%)	7 (6%)	13 (5%)	2 (6%)
Relief												
Alkali	18 (55%)	24 (59%)	7 (63%)	29 (66%)	34 (60%)	6 (55%)	25 (68%)	131 (77%)	10 (77%)	72 (63%)	192 (70%)	23 (66%)
Vomiting	9 (27%)	5 (12%)	0 (0%)	12 (27%)	17 (30%)	1 (9%)	4 (11%)	51 (29%)	1 (8%)	25 (22%)	73 (27%)	2 (6%)
Food	11 (33%)	15 (38%)	3 (27%)	17 (39%)	21 (37%)	4 (36%)	5 (13%)	97 (55%)	5 (39%)	33 (29%)	133 (49%)	12 (35%)
Pressure	0 (0%)	0 (0%)	0 (0%)	3 (7%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	3 (3%)	2 (1%)	0 (0%)
Erectations	0 (0%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)	18 (10%)	0 (0%)	1 (1%)	19 (7%)	0 (0%)

* All percentages are those computed upon the basis of the number of cases judged adequate in clinical data for analysis of other symptoms

may account for the increased frequency of vomiting in cases with such ulcers. Although vomiting was not much more frequently met with in gastric cases in this series, it was in those of Eusterman and Balfour,⁵² Hunt,⁷⁴ Jordan,⁷⁹ Lynch⁹⁴ and Roof.¹²⁷

Physical Findings—Definite physical findings are few. The principal ones are noted in Table VI. Of these, local tenderness was the most consistently found, and this more often in gastric than in duodenal ulcers. Rigidity and spasm were not unusual, while a palpable mass and visible peristalsis were comparatively rare. The findings of Miller, Pendergrass and Andrews¹⁰⁴ closely agree, and this is the usual impression. Hurst and Stewart⁷⁶ stress the diagnostic value of the finding of a localized area of tenderness or hyperesthesia. They found less rigidity and spasm in the absence of pain. The finding of a "tumor" was rather unusual in their experience.

Relief—As is well known, alkali and food, as well as vomiting, may give relief in ulcer patients, and are more effective in duodenal than in gastric ulcers. This is also noted in the reports of Miller, Pendergrass and Andrews¹⁰⁴ and of Roof.¹²⁷ Other sources of relief, mentioned infrequently, were pressure, catharsis, changes of posture and eructations.

Roentgenologic Phenomena—Moynihan¹⁰⁸ states "Of all ancillary methods of diagnosis that of the radiologist should be of the greatest value. In the diagnosis of gastric ulcer it has pride of place, in competent hands it is far more accurate than any other method of diagnosis, clinical or chemical, or than all other methods combined." Not only is the presence of an ulcer to be determined, but the roentgenologist has the opportunity to evaluate the severity of the complications, and the efficacy of treatment. The roentgenologic diagnosis of peptic ulcer depends upon the demonstration of "direct and indirect" signs. The former is the crater, the latter are those due to disturbances in outline or function of the stomach or duodenum.

The pocket formed by a crater is, of all evidence of ulcer, the most definite and the only positive proof (Barclay,¹² Carman,²⁵ Golden⁶³). Its first description is variously ascribed to Reiche¹¹⁹ and to Haudek.⁶⁷ It would seem that Reiche, in 1909, demonstrated the niche in gastric ulcers, and Haudek, in 1912, in duodenal ulcers.

If the gastric ulcer is superficial, involving only the mucosa, the crater may be seen in profile as a small projection beyond the gastric outline, or merely as an opaque spot if on the anterior or posterior surfaces. Such a finding is best obtained with a small amount of opaque medium in the stomach. Radiating mucosal folds may be seen centering about such an area, a finding emphasized by Forssell.⁵⁴ If there is a greater penetration, the niche may be seen as a projection beyond the gastric contour. Its depth is relatively great as compared to its diameter in the majority of instances (Golden⁶³). The depth of a crater shadow may be increased by a heaping up of mucosa around the mouth due to edema, spasm of the muscularis mucosa or scar tissue (Barclay¹²). Such a penetrating ulcer is usually not fixed to the adjacent structures (Hurst and Stewart⁷⁶).

When the ulcer penetrates beyond the gastric musculature, an accessory pocket occurs (Kirklin in Eusterman and Balfour⁵²). In such pockets a fluid level with a superimposed gas bubble may be seen (Kirklin in Eusterman and Balfour,⁵² Golden,⁶³ Holmes and Ruggles⁷¹). If adjacent viscera, most frequently the pancreas and the liver, are invaded by this process, the area may be fixed to palpation, but if it is the gastrohepatic omentum this fixation does not occur (Kirklin in Eusterman and Balfour,⁵² Huist and Stewart⁷⁶). When the liver is the site of such imbedding, the crater may be seen to descend with respiration, a finding not noted in those instances where the pancreas is involved (Kirklin in Eusterman and Balfour⁵²). Failure to visualize these craters may be due to foreign material which acts as a plug, as in a case reported by Stewart and Illick¹⁴⁴. Such foreign material and haste in examining are considered by them to be the causes, most frequently, of failure to visualize gastric ulcer craters.

Twining¹⁴⁸ has emphasized the rolled edges of the benign ulcer crater in contradistinction to the triangular, more or less sharp outline of malignant excavations. Scott,^{132, 133} Rivers and Day,¹²² and Jordan⁷⁹ are among the many who have emphasized the difficulty of differentiating the benign from the carcinomatous niche. Scott,^{132, 133} and Singleton¹³⁵ urge a course of medical treatment and repeated examinations to distinguish between these two conditions, judgment depending upon the presence or absence of healing.

If the crater is on the lesser curvature it is usually readily seen (Huist and Stewart⁷⁶). If the crater is on the anterior or posterior surfaces of the stomach, or if small, considerable painting of the slightly filled viscus may be required before it is seen (Barclay¹²). Pressure and rotation of the patient in order to view the crater in profile are often necessary (Barclay,¹² Golden⁶³). Craters in the region of the cardia may be extremely difficult to demonstrate, palpation often being impossible. A change in position with lowering of the patient's head and a minimal filling may materially aid in its disclosure (Barclay¹²). The niche in an ulcer of the pyloric region is frequently unseen, but variations in the function and appearance of the region should stimulate careful observation (Barclay¹²). Jordan⁷⁹ has pointed out that a loop of intestine, particularly the duodenojejunal flexure, may be confused with lesser curvature craters.

The secondary or indirect evidences of gastric ulcer depend upon disturbances in the physiology of the stomach and often upon deformities resulting from spasm or scarring. An incisura or notching opposite a crater is an infrequent finding and thus is of little diagnostic significance (Golden⁶³). Moreover, it may be due to reflex stimuli from disease of the gallbladder, appendix or duodenum (Carman²⁵). Such an incisura, to be of significant import, must be constant, in the same location, present in all positions assumed during the course of the examination, and withstand manipulation and atropinization (Carman²⁵). If the incisura is deep enough, subsequent fibrosis may result in an "hour-glass" or bilocular stomach. The neck, or channel at the site of the ulcer and incisura, may be more or less permanent (Kirklin

in Eusterman and Balfour,⁵² Golden⁶³) Clairmont³⁰ distinguished the hour-glass deformity associated with annular carcinoma from that due to benign ulcer, describing the displacement of the greater curvature toward the lesser in the benign lesion, and the lesser toward the greater in the presence of carcinoma. This gives rise to the so-called "B" and "X" types of deformity. Roof,¹²⁷ in 1934, recorded an 8 per cent frequency in his gastric ulcer cases. Apparently hour-glass stomachs are now less frequently seen than 10 or 20 years ago (Twining¹⁴⁸).

Gastrospeasm varies greatly in amount and persistence. It may be diffuse or localized, but it is most commonly found in the prepyloric region regardless of the location of the gastric ulcer (Kirklin in Eusterman and Balfour⁵²). This may be attributed to an intrinsic reflex or to inflammatory changes in the pyloric region.

Retention after six hours may or may not be noted. It would seem to be more frequently found in association with gastric than with duodenal ulcers (Roof¹²⁷). Carman²⁵ found it present in 55 per cent of gastric ulcers, and Miller, Pendergrass and Andrews¹⁰⁴ in 60 per cent of all cases. Eusterman⁵⁰ noted retention in 29 per cent of gastric ulcers, 35 per cent of which were sufficiently removed from the pylorus to suggest a reflex phenomenon. In his duodenal cases, retention was slightly less frequent, a percentage of 26. Berkman¹⁵ also found retention more frequently in gastric than in duodenal lesions and he too remarked upon the fact that the pylorus was involved in only 22.7 per cent of gastric and less than 50 per cent of duodenal ulcers. Others who report high frequencies of retention in gastric ulcers include Smithies,¹³⁸ with a percentage of 67, and Chang,²⁹ who set it at 50 per cent. In the analysis of Miller, Pendergrass and Andrews,¹⁰⁴ pylorospasm was present in 48 per cent of gastric ulcers but organic obstruction in only 8 per cent. Alvarez, Horowitz and Ascanio,⁸ in studies on the pyloric muscle, concluded that gastric ulcers generally caused pyloric hypertrophy, but that duodenal ulcers seldom if ever did unless there was actual organic obstruction. This is an interesting commentary upon the possibility of the reflex irritating effect of an ulcer at some distance from the pylorus.

Retention, it should be added, is not diagnostic, in any sense, of the presence of a gastric lesion. Maingot's⁹⁶ synopsis of the conditions leading to gastric retention is interesting in this connection. He divides the causes into general and abdominal. Of the former he lists (a) Nervous and physiologic (*e g*, migraine, melancholia), (b) endogenous toxins (*e g*, nephritis, infections), (c) exogenous toxins (*e g*, emetics). The abdominal causes may be extraperitoneal, such as renal colic, or intraperitoneal, such as peritonitis, cholecystitis, peptic ulcer, neoplasm or pyloric obstruction.

The tone of the stomach may be lowered, a finding more frequently noted in patients whose stomachs have decompensated due to long standing pyloric obstruction (Carman,²⁵ Golden⁶³).

The changes in peristalsis are never characteristic of gastric ulcer. It may be increased (Holmes and Ruggles⁷¹), or weak and irregular (Car-

man²⁵) It may be interrupted at the site of the lesion if the ulcer involves a sufficient depth of tissue (Golden⁶¹) Fiaenkel⁵⁵⁻⁵⁶ described a functional defect in motility which he ascribed to alteration in the activity of the transverse musculature This he considered due to irritation, and described it as a failure of movement of a small segment of gastric contour about an ulcer—an area of flattening of 8 Mm or so in length He called this the “cross-bar sign” It is best seen on serial roentgenograms Miller, Pendergrass and Andrews¹⁰⁴ found peristalsis to be hyperactive in 59 per cent of their gastric cases, but more often so with duodenal ulcers, 65 per cent, suggesting a reflex, nervous association They also reported peristalsis as normal in 15 per cent and sluggish in 22 per cent of their gastric cases, normal in the same per cent, 15, of duodenal and sluggish in 15 per cent

Hyperecretion is sometimes seen as an evidence of irritation or stasis (Golden⁶³)

Pyloric ulcers require somewhat more discussion because of the difficulties attendant upon their diagnosis Barclay¹² bases many obscure diagnoses on secondary phenomena because of the difficulty with which the demonstration of the crater is so often accompanied Local tenderness, hyperperistalsis, intermittent spasm and asymmetry of the pyloric opening into the bulb, have all helped to suggest the presence of an ulcer The latter deformity is more often found with duodenal ulcer than with pyloric It is also described by Keiley⁸³ Stone and Ruggles,¹⁴⁵ discussing the various changes to be noted in the prepyloric and pyloric regions, attributed an eccentric pylorus to either an anatomic variation, adhesions, irregularities in the muscularis mucosa, or an adjacent ulcer

As in the stomach, the demonstration of the barium filled niche is the most certain evidence of ulceration in the duodenum (Åkerlund,² Barclay,¹² Berg,¹⁴ Carman,²⁵ Kirklin in Eusterman and Balfour,⁵² Golden,⁶³ Keiley,⁸³ Kirklin and Burch,⁸⁶ Peter,¹¹⁶ *etc*) A niche without deformity is rare unless the ulcer is extremely superficial (Åkerlund⁴) George and Gerber⁶² expressed the opinion that any duodenal ulcer will deform the duodenum, that a normal bulb on the roentgenogram, therefore, rules out the possibility of any “surgical ulcer” However, craters have been seen without associated deformity (Golden,⁶³ Kirklin in Eusterman and Balfour⁵²) Palpation and pressure play an important rôle in the visualization of the bulb and the maintaining of the shadow of a crater until a roentgenogram can be taken (Barclay¹²) This is often difficult, and the more modern technic of “pressure films” has been a definite aid Using such a technic the number of craters visualized has increased remarkably Åkerlund² advocated such pressure methods because of the frequency of “*en face*” ulcer craters, on the anterior or posterior wall, and because of the possibility of multiple lesions being missed in a fully distended, uncompressed bulb Using such equipment he demonstrated the crater in 60 per cent and 75 per cent of cases as noted in two reports (Åkerlund³ 4), Berg¹⁴ noted a crater in 50 per cent of duodenal ulcers,

Diamond⁴³ in 66.6 per cent, Clark and Geyman³¹ 54 per cent and Ettinger and Davis⁴⁹ in 50 per cent. Golden⁶³ stated that craters are demonstrable in 50 to 60 per cent of cases with special methods and in 13 to 15 per cent without. Cairman²⁴ used no pressure apparatus and had a frequency of demonstration of a crater in duodenal ulcers of 27 per cent, while Kirklin,⁸⁴ and Kirklin and Burch,⁸⁶ showed them in 15 and 17 per cent of two series. In the latter report⁸⁶ they stated that a crater must retain its position despite heavy palpation to be definitely diagnostic. They felt that the higher frequency of niche demonstration with pressure apparatus was undoubtedly real, but could lead to errors in other directions. For example, such a technic might lead to the diagnosis of a crater when there was present a cicatricial sacculation, pseudo-diverticulum or merely a fleck of barium caught between the folds of the mucosa. They also felt that the discrepancy in crater frequencies might be due to the criteria used, or the source of material studied. For example, they found higher percentages in surgical cases, and only 25 per cent of duodenal ulcers (140 cases in all) at necropsy showed definite craters. Kirklin and Burch, however, stress the importance of the niche diagnosis and add this differential suggestion. A niche means an ulcer if deformity is present, an active ulcer if there is also irritability, and an improving ulcer if it grows smaller or disappears. Holmes and Schatzki,⁷³ it might be added, feel that the distortion of the mucosal relief about a niche is of greater importance and more conclusive evidence of the presence of a crater. A "halo" of swollen mucosa about the crater has been described by Peter,¹¹⁶ and a heaping up to increase the apparent depth of penetration has been noted here as in the stomach (Barclay¹²).

Of the indirect signs, distortion of the bulbar outline and of its mucosal pattern are so prevalent that they may well be considered direct evidence. These were first described by Cole³³ and ascribed by him to the presence of a duodenal ulcer. Such a deformity of the bulb may be due to other causes, including incomplete filling, periduodenal adhesions secondary to upper, right quadrant inflammatory processes (particularly gallbladder disease), neoplasm, spasm from extrinsic sources, duodenitis and healed ulcer (Kirklin in Eusterman and Balfour,⁵² Cordiner and Calthrop³⁴). Still, the aggregate of all these causes is small and should seldom lead to an incorrect diagnosis (Kirklin in Eusterman and Balfour⁵²). Åkerlund⁴ indicated that the confusing irregularities in bulbar outline could usually be sufficiently clarified in order to reach a diagnosis. Thus a rounded shadow due to the impression of the gallbladder can usually be moved on pressure or may be differentiated on rotating the patient. Such a deformity is usually seen in the distal bulb, and can, in the last analysis, be excluded by a gallbladder series employing tetraiodophenolphthalein. Periduodenal adhesions result in a decreased mobility of the bulb, and the deformity is somewhat atypical. New growths are rare, benign lesions such as polyp giving a rounded shadow. Congenital diverticula seldom arise from the bulbar portion of the duodenum, and if projected from the second portion in a confusing manner can often be displaced by manipula-

tion or rotation Barclay¹² states that a positive diagnosis is usually correct if based on deformity alone, but never certain unless the niche is also seen.

Deformity of the bulb is the result of spasm and scarring (Berg,¹⁴ Kohler,⁸⁷ Sutherland¹¹⁷). With the spasm limited to the muscularis mucosa, a star formation of radiating lines may result (Beig,¹⁴ Golden,⁶³ Holmes and Ruggles,⁷¹ Peter¹¹⁶). More often the outer musculature is involved to some degree. Opposite the crater an incision, similar to that found in the stomach, may be seen (Beig,¹⁴ Kirklin in Eusterman and Balfour,⁵² Peter¹¹⁶). No more than a loss of the normal convexity of the bulb may be noted in the area around the crater (Peter¹¹⁶). By far the greater number of duodenal ulcers, however, are associated with a marked, often bizarre outline.

The bulb may be shortened markedly, or narrowed to a thin channel (Åkerlund,⁴ Beig,¹⁴ Kohler,⁸⁷ Peter¹¹⁶). Pseudodiverticula, or pouches with the crater at the stoma, may arise due to contraction of scar tissue bands and the pulsion activity of food (Åkerlund²). As previously mentioned, an eccentric position for the opening of the pylorus into the bulb is more frequently seen with duodenal ulcer than with pyloric.

Carman²⁵ classified bulbar deformities as (1) General, (2) basal border, (3) crater, (4) incisural, (5) contracted, (6) accessory pocket, and (7) pseudodiverticula. These correspond to the grouping of Åkerlund,⁴ who notes six main types: (1) Niche, (2) transverse encroachments, (3) longitudinal restrictions (such as shortening of the bulb), (4) pouch formation (due to sacculation), (5) pseudodiverticula, and (6) relief deformities (such as due to spasm and hypertrophy of the muscularis mucosa).

In the presence of an ulcer the duodenal bulb is very apt to be irritable and hyperactive, emptying rapidly and often rendering visualization difficult. Reflexly gastric peristalsis, tone and motility are all apt to be increased (Carman,²⁵ Golden,⁶³ Holmes and Ruggles,⁷¹ Kohler⁸⁷). In consequence, gastric emptying may be very rapid. However, if the ulcer crater is near the pylorus a marked pylorospasm may result, and delay in emptying be noted (Golden⁶³). Such spasm and obstruction due to actual scarring in the bulb account for the retention noted in the stomachs of duodenal ulcer patients. As discussed under gastric ulcers, this is usually less marked than in lesions of the stomach, less than 50 per cent of cases showing a six hour retention (Golden⁶³).

Duodenal stasis has been noted frequently in association with duodenal ulcer and Friedenwald and Feldman⁵⁸ urged the exclusion of such a lesion in the presence of this finding. Duodenal ulcer accounted for delay in emptying of the second portion in 44 per cent of 80 instances of "puddling."

Tenderness definitely localized to the bulb may or may not be present (Åkerlund,⁴ Golden⁶³).

Some of the sources of error in the roentgenologic diagnosis of the stomach and duodenum have been suggested in the foregoing paragraphs.

Others include the presence of hypertrophied folds, particularly the prepyloric fold, which has led to a false diagnosis of crater (Kirklin,⁸⁵ Golden⁶³) Irregularities of the entire upper gastro-intestinal tract may be found in association with a closely approximated loop of colon, with ascites, pregnancy and intra-abdominal tumors (Kirklin⁸⁵) A crater may be plugged by mucus, blood, food, or hypertrophied and edematous folds in the duodenum as well as in the stomach (Åkerlund,⁴ Cordiner and Calthrop³⁴) Small anterior or posterior wall duodenal ulcers may fail of detection as well as those in the distal bulb (Kirklin⁸⁴) In duodenitis a fleeting glimpse of the bulb may cause an ulcer to be overlooked (Kirklin⁸⁴) In this connection Garland⁶¹ stated that in a roentgenologically negative bulb associated with positive clinical symptoms, if the symptoms are acute an ulcer may have been missed, and if they are chronic, they probably did not have an ulcer as their cause When one of two ulcers or lesions is seen, an incomplete diagnosis may result Pyloric block, so complete that the pylorus or the bulb cannot be properly visualized, may allow no more than the impression of "pyloric obstruction"

The stomach is readily responsive to irregularities of the nervous system and the endocrines, as well as toxic states and infections in remote organs As a result, it must be with caution that physiologic changes are interpreted as evidence by themselves, of intrinsic disease (Eusterman⁵¹) Boyd²¹ describes the stomach as weeping for its neighbors, and often so overdoing it as to obscure the basic source of trouble

Despite these potential sources of error the accuracy with which the trained roentgenologist detects duodenal and gastric lesions is very great Carman²⁶ reports accurate diagnoses in 96 per cent of peptic ulcers Emery and Monroe⁴⁸ in 93 per cent, and Blackford and Dwyer¹⁷ in 83 per cent Smithies¹³⁸ accuracy was 85 per cent in gastric cases, while that of Miller, Pendergrass and Andrews¹⁰⁴ was 94 per cent in duodenal and 88 per cent in gastric

Table VII records the roentgenologic findings in this series These cases were examined by workers of greatly varying experience in roentgenologic methods There did not appear to be any association between the position of the stomach and the presence of ulcer Irregular, sluggish and absent peristalsis was more frequently recorded in association with gastric than with duodenal ulcers, but this disturbance in physiology was not consistent enough

In accord with the findings of others, retention was more marked in patients with gastric ulcers than in the duodenal or combined ulcer groups This was also true of delay in emptying as seen fluoroscopically When retention was found, the portion of the motor meal, which was present after six hours, was greatest in the combined ulcer cases, being almost twice the amount estimated in the other groups In this connection it is of interest that pylorospasm was noted less frequently in the gastric group, indicating that such an obstruction probably does not account for retention as often as disturbed motility and peristalsis

A lesion was seen in 320 (98 per cent) of the 326 cases examined roent-

TABLE VII
RÉSUMÉ AND ANALYSIS OF ROENTGENOLOGIC FINDINGS

	Medical Pathology			Surgical Pathology			Cebotomy			Totals		
	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb	G U	D U	Comb
Roentgenologic Findings												
Number of Cases	23 (30%)	27 (34%)	10 (52%)	35 (80%)	41 (68%)	8 (73%)	17 (45%)	154 (85%)	11 (85%)	75 (47%)	222 (70%)	29 (68%)
Position of Stomach												
High	3 (13%)	5 (18%)	3 (30%)	2 (6%)	6 (15%)	2 (25%)	3 (18%)	12 (8%)	3 (27%)	8 (11%)	23 (15%)	8 (27%)
Low	4 (17%)	8 (30%)	1 (10%)	12 (32%)	12 (29%)	2 (25%)	2 (11%)	38 (25%)	5 (45%)	18 (24%)	58 (27%)	8 (27%)
Medium	6 (26%)	14 (52%)	6 (60%)	21 (60%)	24 (56%)	4 (50%)	12 (71%)	104 (68%)	3 (27%)	39 (52%)	141 (64%)	13 (45%)
Peristalsis												
Normal	9 (39%)	12 (45%)	4 (40%)	11 (31%)	15 (37%)	2 (25%)	1 (24%)	70 (46%)	4 (36%)	24 (33%)	97 (44%)	10 (33%)
Delayed	4 (17%)	4 (15%)	0 (0%)	2 (6%)	5 (12%)	1 (13%)	3 (18%)	10 (7%)	2 (18%)	9 (2%)	19 (9%)	3 (10%)
Irregular	6 (26%)	5 (18%)	4 (40%)	13 (44%)	17 (41%)	5 (63%)	7 (41%)	38 (25%)	2 (18%)	26 (36%)	60 (27%)	11 (38%)
Sluggish	5 (22%)	3 (11%)	3 (30%)	12 (32%)	8 (20%)	4 (50%)	5 (29%)	21 (16%)	4 (36%)	22 (31%)	35 (16%)	11 (38%)
Hyperactive	4 (17%)	4 (15%)	4 (40%)	2 (6%)	7 (17%)	0 (0%)	2 (12%)	16 (10%)	2 (18%)	8 (11%)	27 (12%)	6 (21%)
Constricting	0 (0%)	1 (4%)	0 (0%)	1 (3%)	3 (7%)	0 (0%)	0 (0%)	5 (3%)	0 (0%)	1 (1%)	9 (4%)	0 (0%)
Ineffective	1 (4%)	3 (11%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	6 (4%)	3 (27%)	1 (1%)	10 (5%)	3 (10%)
Reversed	0 (0%)	1 (4%)	0 (0%)	4 (12%)	3 (7%)	2 (25%)	0 (0%)	8 (5%)	1 (9%)	4 (5%)	12 (5%)	3 (10%)
Absent	1 (4%)	1 (4%)	1 (10%)	2 (6%)	0 (0%)	0 (0%)	2 (12%)	5 (3%)	0 (0%)	5 (7%)	6 (3%)	1 (3%)
Gigantic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (2%)	0 (0%)	0 (0%)	3 (1%)	0 (0%)
Emptying												
Normal	7 (30%)	16 (59%)	3 (30%)	14 (40%)	25 (61%)	3 (38%)	1 (24%)	76 (49%)	3 (27%)	25 (33%)	117 (53%)	9 (31%)
Delayed	5 (22%)	6 (22%)	3 (30%)	17 (49%)	12 (29%)	3 (38%)	12 (71%)	66 (43%)	7 (61%)	34 (45%)	84 (38%)	13 (45%)
Slow	0 (0%)	1 (4%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	4 (3%)	0 (0%)	0 (0%)	6 (3%)	0 (0%)
Rapid	3 (13%)	0 (0%)	0 (0%)	3 (9%)	1 (2%)	0 (0%)	0 (0%)	2 (1%)	0 (0%)	6 (8%)	3 (1%)	0 (0%)
Little	0 (0%)	1 (4%)	0 (0%)	1 (3%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	3 (1%)	0 (0%)
None seen	0 (0%)	1 (4%)	2 (20%)	1 (3%)	0 (0%)	1 (13%)	1 (24%)	2 (1%)	1 (9%)	5 (7%)	3 (1%)	4 (14%)
Retention												
Cases showing	11 (48%)	9 (33%)	4 (40%)	19 (54%)	16 (39%)	3 (38%)	16 (94%)	69 (15%)	6 (55%)	46 (61%)	94 (42%)	13 (45%)
Average percentage of 6 hr meal retention	41%	67%	83%	35%	18%	24%	38%	36%	75%	36%	41%	66%
Local Findings												
Stomach												
Pylorospasm	7 (30%)	10 (37%)	5 (50%)	7 (20%)	8 (20%)	2 (25%)	2 (12%)	32 (21%)	2 (18%)	16 (21%)	50 (21%)	9 (31%)
Evaginated mucosal folds	2 (9%)	4 (15%)	2 (20%)	6 (17%)	3 (7%)	1 (13%)	3 (18%)	8 (5%)	2 (18%)	11 (14%)	15 (7%)	5 (17%)
Crater	14 (60%)	1 (4%)	1 (10%)	27 (78%)	2 (5%)	2 (25%)	12 (71%)	1 (1%)	5 (15%)	53 (71%)	4 (2%)	8 (28%)
Incisura	6 (26%)	0 (0%)	2 (20%)	8 (23%)	3 (7%)	0 (0%)	1 (6%)	0 (0%)	0 (0%)	15 (20%)	3 (1%)	2 (7%)
Irregularity	1 (4%)	0 (0%)	2 (20%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	2 (1%)	2 (7%)
Filling defect	4 (17%)	0 (0%)	0 (0%)	9 (26%)	1 (2%)	1 (13%)	5 (29%)	0 (0%)	0 (0%)	18 (24%)	1 (0.5%)	1 (3%)

genologically The finding of a crater led to the diagnosis of gastric ulcer in 53 of the 60 cases correctly interpreted Of the remaining seven instances, three were prepyloric ulcers in which antial spasm led to the diagnosis although no crater was seen Two were "hour-glass" stomachs in which the crater could not be demonstrated One was a healed ulcer which had caused a defect or stiffness in the gastric contour, and the last was an ulcer in the pylorus, causing complete obstruction and retention Of the duodenal ulcers, a crater was seen in 24 per cent of instances This is the usual figure where no special technics are used In all other patients with duodenal ulcer the roentgenologic diagnosis was made when bulbar deformity was seen

Two hundred eighty-eight of the 326 cases were accurately diagnosed (88 per cent) Ninety-five per cent of the duodenal cases were correct, 80 per cent of the gastric, and 55 per cent of the combined About one-third of all the errors fell in this last group, 13 cases in all In 12 of these the error was in failure to see both lesions Ten of the 12 "missed" ulcers were gastric, and craters could be seen on reviewing the roentgenograms in nine instances The other two "missed" ulcers were duodenal, one of which had caused bulbar deformity which was seen on reviewing the films The other error in the combined group was in a case in which the ulcer involved the pylorus, an impression that the lesion was malignant having been given

Three gastric and three duodenal ulcers were not seen One gastric diverticulum, and the markedly hypertrophied folds associated with ulcer, were considered as ulcer and polyp respectively In the bulb one ulcer was called a diverticulum and another was attributed to periduodenal adhesions A third case had a deformed bulb due to an ulcer which was thought to be due to external pressure The remaining errors shown in Table VII are self-explanatory

SUMMARY—An analysis of 520 ulcer patients has been presented Insofar as possible comparable findings from similar material examined by others has been recorded, and the opinions of the writers noted Comment has been made, where possible, on the association of the clinical, pathologic and roentgenologic findings

It is recognized that this group of cases is selective and cannot, therefore, be considered as giving "typical" statistics This shortcoming, however, is somewhat overbalanced in that the cases are all "proven" In order that the source of each finding may be judged, the tables include the results of the analyses of autopsy and operated cases

CONCLUSIONS

It would seem, from this study, that

(1) Statistics relative to peptic ulcer vary considerably, due to the source of the material and the interpretation of the author

(2) Ulcers arise in an area of alimentary tract mucosa where the resistance has been lowered and where gastric juice may exert an injurious effect

(3) Peptic ulcers occur in from 1 to 2 per cent of the population as a

whole, and in about the same frequency in general hospital admissions. They are encountered about three times as often as this in postmortem studies.

(4) Both duodenal and gastric ulcers are more frequent in men than in women.

(5) There is no racial selectivity.

(6) Patients with gastric ulcer averaged older than those with duodenal ulcer, and the peak incidence was between 40 and 50 years of age.

(7) Duodenal ulcers are more frequent than gastric. Acute ulcers are more frequent in the stomach than in the duodenum, which may account for the discrepancy between clinical and pathologic statistics.

(8) Ulcers of both the stomach and the duodenum are present in about 10 per cent of ulcer patients.

(9) Pathologically, gastric and duodenal ulcers are essentially similar.

(10) Benign gastric ulcers are more frequent on the lesser curvature, within 5 cm of the pylorus.

(11) Duodenal ulcers are more frequent within 1 cm of the pylorus, and are practically limited to the bulb.

(12) Gastric ulcer craters are usually less than 3 cm in diameter and those of duodenal ulcers are usually under 1 cm.

(13) Perforation occurs in about 5 to 10 per cent of hospitalized peptic ulcer cases.

(14) Hemorrhage of some degree is present in about 20 per cent of hospitalized ulcer patients and in 10 per cent of all ulcer cases.

(15) Carcinoma arises in gastric ulcer in 5 to 10 per cent of cases.

(16) The mortality due directly to peptic ulcers is about 2 to 5 per cent.

(17) No direct association between disease of the gallbladder or appendix and peptic ulcer could be demonstrated.

(18) The symptomatology of peptic ulcer is marked by remissions and exacerbations, and is subject to seasonal variations.

(19) Pain, the most important symptom of peptic ulcer, bears a definite relationship to eating. It occurs earlier in gastric than in duodenal lesions.

(20) Local tenderness is the most constant physical finding in peptic ulcer patients.

(21) The diagnosis of duodenal ulcer roentgenologically depends upon the demonstration of a definite crater or a deformed bulb. The diagnosis of gastric ulcer depends upon the demonstration of a crater and of abnormal physiologic behavior or deformed anatomic structure.

(22) Retention after six hours is more frequent in the presence of gastric than of duodenal ulcers, although the amount of retention is slightly greater in the latter. Gastric ulcers which cause retention may be remote from the pyloric ring.

(23) Gastric peristalsis is apt to be hyperactive in the presence of a duodenal ulcer, and gastric tone and motility may be increased.

(24) Duodenal ulcer causes spasm and scarring in the bulb, and the deformity so produced is almost always due to such a lesion.

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CHANGING METHODS IN THE SURGICAL TREATMENT OF PEPTIC ULCER*

A STUDY OF THE CASES OPERATED UPON AT THE ROOSEVELT HOSPITAL,
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IN NO field of surgery has there been displayed a greater interest than in that of the treatment of ulcers of the stomach and duodenum, and in none, during recent years particularly, has there been manifested a wider divergence of opinion. The story of ulcer surgery is not, in point of time, a long one, but in its brief course, several significant changes in point of view have occurred.

It may be of interest to review a part of this story, considering these changes, as illustrated by the experience of one hospital—the Roosevelt. As a result of clinical experience through the years, how do our policies and procedures in relation to peptic ulcer differ now from those of an earlier day? What has brought about these changes in our attitude toward this problem?

It is not presumed to attempt here, by the presentation of a great amount of clinical material, nor of a mass of statistical data, to prove the validity of any particular therapeutic method, nor even to justify, on such a basis, the position in which we now stand. The purpose of this paper is merely to record the events of a clinical experience which we believe to be fairly typical, and which may serve to indicate the trend and progress of peptic ulcer therapy.

Major surgery of the stomach is so much an accepted matter of usage to-day that it is a little difficult to realize how short a distance we are from its beginnings. In Ashurst's International Encyclopedia of Surgery, published in 1884, Henry A. Morris¹ had this to say concerning it: "Gastro-enterostomy is an operation which has been proposed for those cases of cancer of the pylorus in which excision is not possible. It was performed for the first time by Dr. Anton Wolflei, in Vienna, and has since been repeated by Billroth. This mode of treatment appears to have been devised on the spur of the moment, after an exploratory incision had been made in the abdomen of a man who was suffering from cancer of the pylorus, and in whom the operation for removal of the tumor proved to be impossible." Report of this case was published in 1881. Partial gastrectomy, or pylorectomy, was first performed by Péan of Paris, in 1874, but his patient died on the fifth day. He continues: "The first successful results were obtained by Billroth and Wolflei. Though it has now been performed 30 times or more, the operation still has about it so much of the nature of an experiment—perhaps even of a mere surgical exercise—that it is not possible to describe it as a thoroughly recognized surgical

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proceeding ” It has been proposed, he said, for cancer and cicatricial stenosis of the pylorus “with most disastrous consequences ” “Twice at least, and successfully, it has been done for simple chronic gastric ulcer, and once, also successfully, for stricture of the pylorus following penetrating ulcer ”

What advances occurred during the succeeding 20 years in technic, and hence in surgical boldness in attacking the problem of peptic ulcer, may be gathered from a paper by Brewer,² in 1907, entitled “A Critical Review of a Recent Series of Operations Upon the Stomach ” In it, he reported 17 cases of suspected peptic ulcer operated upon by him at the Roosevelt Hospital Of these, 12 showed anatomic lesions while five did not, the diagnosis having been made purely upon clinical observation He deplored the lack of a certain method of diagnosis, and propounded, as a result of his experience, the following indications for the treatment of benign lesions of the stomach

- (1) Intelligent medical treatment in all primary cases of simple round ulcer If unrelieved after six weeks of this treatment, operation should be advised
- (2) Operation in all cases of indurated chronic ulcer, and in all cases of recurrent symptoms after primary cure
- (3) Operation in all cases of pyloric stenosis, excepting those due to gummatous infiltration

Rodman,³ in 1914, drew a sharp distinction between the treatment of gastric and of duodenal ulcerations He had advocated, since 1900, the employment of pylorotomy and partial gastrectomy or excision of the ulcer bearing area in the treatment of gastric ulcer, especially in the pyloric region He condemned the use of gastro-enterostomy alone in the treatment of these lesions, feeling that it failed to protect against the dangers of carcinoma, hemorrhage, and perforation He had collected and published, at the same time, reports of 205 pylorotomies, with 18 deaths, a mortality of 8.7 per cent Of local ulcer excisions, there were 171, with three deaths, or 1.75 per cent

During the years 1912–1914, the writer assisted at an interesting and significant series of observations then being conducted by Brewer and Cole⁴ The question raised was “Is there reason to believe from our present experience that the roentgen ray will eventually prove as valuable for the diagnosis of surgical lesions of the stomach and duodenum as for the diagnosis of fractures and urinary calculi ?” The lack of a certain diagnostic procedure, which he had deplored in his earlier paper, had continued to trouble Brewer, and in characteristic fashion he had proceeded to do something about it The results seemed to give an affirmative answer to the question While the first roentgenograms of the stomach employing contrast medium were reported by Hemmeter, in 1896, Cole now added the principle of serial pictures, which greatly increased the value and accuracy of the studies

Brewer and Cole reported 27 cases, which had been studied and operated upon In 22 cases, in which a definite diagnosis was made roentgenologically, 20 showed the diagnosis to have been correct Of five cases in which an

opinion only was expressed, based upon the roentgenologic findings, four showed the opinion to have been correct. The gross result was 89 per cent accurate diagnoses.

This striking advance in diagnostic accuracy was not hailed with complete enthusiasm in all quarters. There was some difference of opinion as to its value. Bevan, for instance, in discussion of the paper, said of the roentgenologic method of diagnosis: "It is of very little value in duodenal ulcer, in not one case out of ten is it of value."

It is certain, in any event, that the diagnostic aid offered by roentgenologic examination materially increased, in our institution at least, the activity of stomach surgery. In 1915, Peck⁷ reported 134 operations upon the stomach for benign lesions, performed at the Roosevelt between 1910 and 1915. They were for: Chronic duodenal ulcer, 74; chronic gastric ulcer, 24; chronic gastric ulcer with hour-glass deformity, six; perforated duodenal ulcer, 17 (a surprisingly low figure, comparatively), and perforated gastric ulcer, 13. He observed that modern surgeons of our time have "made safe and a matter of routine operations which a few brief years ago were hazardous in the extreme and uncertain of outcome." He pointed out that at the Roosevelt Hospital gastro-enterostomy had been the routine treatment of chronic ulcer of the duodenum, and that pyloric exclusion or excision of the ulcer had been rarely resorted to. Gastro-enterostomy had, in fact, been performed in 72 of the 74 cases of duodenal ulcer (one pylorotomy and one exclusion accounted for the other two). There had been six deaths, or 8.1 per cent mortality. He reported 58 of these cases traced subsequently. Of these, 51 had remained cured, five improved, and two were unimproved. Thus, he estimated 68.9 per cent of all operated upon as cured, and 88 per cent of those traced. He encountered no case of gastrojejunal ulceration.

In accord with Rodman and earlier authors, he preferred excision in the treatment of gastric ulcers. Of the 30 he reported, 13 received gastro-enterostomies, and the remaining 17 had partial gastrectomies or local excision or cauterization in addition. Of the 13 simple gastro-enterostomies, two died after operation, two "subsequently," one developed carcinoma, one was unimproved, and seven were well seven months to five years afterwards. He concluded that for gastric ulcers at or near the pylorus, a pylorotomy was best, while for those situated on the lesser curvature in the pyloric or middle third areas, local excision, preferably with gastro-enterostomy, was indicated. A good gastro-enterostomy stoma, he believed, would continue to function in spite of a patent pylorus, and a functioning stoma would usually be accompanied by a clinical cure.

The succeeding ten years marked a period of great activity in the surgical treatment of gastric and duodenal ulcer at the Roosevelt Hospital. With the benefit of quite accurate roentgenologic diagnosis, an improved operative technique and the assurance gained from the observation of satisfactory results, an increasing number of cases were submitted to operation. Over a period of ten years, from 1917-1927, an average of 50 cases a year were operated

upon The great majority of these were cases of duodenal ulcer, upon which 412 gastro-enterostomies were performed It was the exception, during this period, that such cases received preliminary medical treatment, at least in the hospital Customarily, the diagnosis having been established by clinical findings and roentgenologic examinations, operation was performed rather promptly The feeling prevailed, at least among the surgeons, that peptic ulcer was essentially a surgical disease and that the surgical treatment accorded it was in the main satisfactory

It is undoubtedly true that among medical men and gastro-enterologists, at least, this attitude was seriously questioned Among others, it will be remembered, Bastedo, in this city, valiantly upheld the claims of medical treatment The literature of the time reflects the controversy which raged between the proponents of the two types of treatment in all parts of the country As time elapsed, it became increasingly evident that the claims for medical treatment in peptic ulcer, supported by a growing mass of reported results, were not to be denied

Peck⁶ recognized this clearly, and stated, in 1924, that "We agree with the internists that early, uncomplicated cases (of duodenal ulcer) should first receive medical treatment and that a considerable number of patients are cured, or at least kept in reasonable comfort for long periods of time We prefer that patients should have had a thorough and intelligent trial of medical treatment before surgery is considered"

In this paper, he brought up to date his report on the results of his ulcer surgery at the Roosevelt Hospital Since his previous report on 74 cases, in 1914, he had operated upon 122 additional cases of chronic duodenal ulcer, or 196 in all Gastro-enterostomy had been performed in 191 cases, pylorectomy in three, pyloric exclusion in one, and simple excision in one Sixteen deaths occurred in this group, a mortality of 8 per cent As to late results, one case was reoperated upon for gastrojejunal ulcer, and one, after eight years, for a "rigid stoma" Four patients had recurrence of pain and indigestion

As a result of this continued experience, he stipulated his choice of procedure in various types of duodenal ulcer (1) Small, single, anterior wall ulcers without narrowing of the gut might have local excision without gastro-enterostomy (2) Chronic, indurated ulcers, without obstruction, including the chronic perforating variety, might be treated by gastro-enterostomy which, alone, would cure a large percentage In the more severe cases, a two-stage operation might be employed (gastro-enterostomy, followed by resection 10 to 14 days later) as a safer and easier method than primary resection (3) For cases with duodenal stricture or so-called pyloric stenosis, gastro-enterostomy was ideal (4) For cases in which severe hemorrhage had occurred, a gastro-enterostomy plus excision of the ulcer area was advocated

In these recommendations, a trend toward a slightly more radical attitude begins to be apparent, though Peck was by no means ready to accept the teachings of some of his contemporaries In fact, in this paper he said "We have

been considerably disturbed by the tenor of several papers and discussions, and the attitude of a number of prominent surgeons, as expressed at recent important meetings, notably in the New York Surgical Society, during the past year. The attitude which disturbed us was the tendency to advocate radical measures of resection, often of large portions of the healthy stomach, for the surgical cure of this disease. "Our own experience and belief is," he continued, "that simple gastro-enterostomy, properly performed, is curative and adequate in the great majority of chronic duodenal ulcers. That from 80 to 90 per cent of the patients so treated are completely relieved of their symptoms and remain well as they are followed year after year." Further "We do not believe that gastro-enterostomy should go into the discard in the treatment of duodenal ulcer, nor do we believe that extensive resections of normal stomach are justifiable for this lesion." And again "We are unconvinced that resection to prevent the formation of gastrojejunal ulcer is a proper procedure in the 98 cases who do not need it to possibly avoid its occurrence in the other two."

His attitude in the matter of gastric ulcer was quite different as, in fact, had been that of almost all surgeons since Rodman's earlier observations. In this same paper, Peck reported on 72 cases of gastric ulcer operated upon since 1910. He did not analyze these cases in detail, but expressed his opinion concerning their appropriate treatment. "Eradication of the ulcer should be a part of whatever operative procedure is adopted," he said. He advocated usually a local excision of the ulcer or its cauterization with a gastro-enterostomy added. Gastro-enterostomy alone, he felt, would fail to effect a cure in many cases, and apprehended the risk of malignancy. In many instances, however, where excision might prove too severe for the patient, a gastro-enterostomy would be palliative, sometimes curative. In ulcers near the pylorus, he felt that partial gastrectomy was usually the best procedure.

I have dwelt at some length upon this paper of Peck's, not only because it represents the prevailing attitude at that time, but also because it expresses the philosophy upon which the treatment of peptic ulcer at the Roosevelt Hospital was then based, and upon which our method and teaching were predicated for many years. With this point of departure, accepting this point of view as fixed, let us carry forward the record of ulcer treatment at the Roosevelt Hospital, bringing Peck's report up to date.

Since Peck's report, that is from 1924 through 1937, there have been operated upon at the Roosevelt Hospital 262 cases (269 operations) for chronic ulcers of the stomach and duodenum, exclusive of operations for acute perforations of primary ulcers. It is of interest to observe that year by year the number of operations performed for these conditions has gradually diminished, and this without a significant diminution of the number of cases admitted. In 1926, for instance, there were 46 such operations, in 1936, but 12. This change has been due primarily to the increasing recognition of the fact on the part of the surgeons that careful medical management is capable of relieving or controlling a very considerable number of these cases. Sandweiss⁷

has recently pointed out, following a careful study of 291 cases, that 90 per cent were rendered symptom-free after a diet-alkali-rest regimen, and that 60 per cent of those resisting this form of treatment responded to some other type of nonsurgical management (injection treatment, release of "tensional states") We have, as the result of experience and observation, come to the same conclusion as Rankin⁸ who says that "The surgical treatment of peptic ulcer is the treatment of its complications"—obstruction, perforation, repeated hemorrhage, intractability, questionable malignant degeneration We feel, as does he, that surgery is indicated only in cases where the medical regimen has failed, or where the above complications have resulted

In fact, it is our practice now to consider all cases of chronic peptic ulcer as medical problems, primarily, and to admit them directly to the medical wards In this, we are but carrying to its logical end the principle enunciated by Brewer, in 1907, and reaffirmed by Peck, in 1924 In the development of this policy, a considerable change has gradually taken place in our census of ulcer patients While in the period from 1914-1924, the average admission of chronic ulcer cases to the surgical wards was 39 per year, and to the medical wards 11 per year, in 1931 the medical wards were receiving 60 per year and the surgical 26 This change has been fully justified by the results obtained in simple primary duodenal and gastric ulcer by medical treatment The records of the medical service show that 170 of 192 cases, or 88 per cent, of primary peptic ulcer admitted during the last five years were discharged symptom-free We are in substantial agreement with Ochsner,⁹ when he says "It is our firm conviction that there is no surgical treatment of peptic ulcer, and that surgery is indicated only when there are complications"

Not only is no patient now operated upon at the Roosevelt Hospital for chronic peptic ulcer without having had a thorough, controlled, and efficient course of medical management, but each case for whom operation is proposed must be passed upon by a "court" consisting of physician, surgeon, gastroenterologist, and roentgenologist By this method of conservatism, the patient is given the full benefit of a thorough survey of his problem In these conferences, we find ourselves guided to our conclusion as to the appropriateness of operation first by the patient's age and a consideration of his general condition, next, by the diagnosis of his lesion, determined as accurately as possible by a combined study of his history, physical and laboratory findings, and roentgenologic examination, next, by a careful evaluation of the rationale and thoroughness of his previous course of treatment, and finally, the generally accepted criteria for the necessity of operation, so well expressed by Lahey,¹⁰ are applied (1) The persistence of pain in spite of a good trial of adequate medical management (2) Persistent or recurrent pyloric obstruction (3) Massive, recurrent hemorrhage in which fatality is threatened (4) When recurrent hemorrhage occurs, even if symptoms are controlled by treatment (5) When a lesion of the stomach proves intractable to adequate treatment or suggests the presence of malignancy In applying these five criteria, we give considerable weight to the changes in appearance of the lesion

by roentgenologic study, as supplementing our interpretation of clinical response

This plan, as now practiced, has been of gradual development. In studying our operated cases since 1924, it is impossible to fix a date upon which this plan became effective in controlling our procedures. These, it will be seen, have undergone a slow but steady change. Due, in large measure, to the application of these principles, there has been a gradual decline in our utilization of the less radical surgical measures. The intractable type of cases accepted for operation have, in other words, demanded, for the most part, more radical surgery (as Peck himself recognized in his paper in 1924) than was previously accorded to the simple ulcer cases when more were being operated upon. Thus, for instance, while from 1924-1937, 148 gastro-enterostomies were performed, they show, year by year, a gradual diminution. The record for ten years of this operation for duodenal ulcer was as follows: 1926, 27, 1928, ten, 1930, six, 1932, three, 1934, two. The resection type of operation (Polya and Billroth II) for this lesion has shown, on the other hand, a gradual increase. For example: 1927, one, 1929, two, 1935, three, 1936, four.

A study of the entire group of operations during this period may be interesting for comparison with the earlier group, as indicating certain other trends in our approach to the problem. Table I shows the number and results of operations upon cases of chronic duodenal ulcer. Gastro-enterostomy, it will be seen, far outnumbers the other operations. Its good results compare fairly well with Peck's earlier series, its bad results (16 per cent) are nearly the same, and its mortality (6 per cent) a little less. The late results, in all instances, are determined upon the basis of at least a year of postoperative observation, some run as long as nine years.

TABLE I

CHRONIC DUODENAL ULCER

Operation	Num- ber	Good Results		Poor Results	Died	Percentage
		Early	Late			
Gastro-enterostomy	148	45	71	24	9	6
Pyloric operations (Horsley, Finney, Judd)	21	5	12	4	0	
Polya	10	3	7	0	0	
Billroth I	1			1		

Table II analyzes the poor late results of these operations, and indicates the causes of deaths in each, and the early postoperative surgical complications encountered. The single case of Billroth I proved disappointing, developing obstruction at the stoma one year later and requiring gastro-enterostomy, as did one Horsley procedure six months after its performance. It is reasonable to suppose that these late difficulties may have been due to technical imperfections in the original procedures. With the one exception noted, the pyloroplastic operations gave good results and were unattended by either late or early complications as far as they have been followed. The Polya opera-

tions, though few, had no mortality, and as yet no complications, though three of the ten have not been traced

TABLE II
CHRONIC DUODENAL ULCER

	Gastro- enterostomy (148)	Pyloro- plasty (20)	Polya (10)	Billroth I (1)
Early Surgical Complications (Survived)	(11)			
Hemorrhage (postoperative)	1			
Obstruction (+ entero-enterostomy)	7			
Abscess	1			
Evisceration	2			
Causes of Death	(9)			
Peritonitis	3			
Embolism	1			
Shock	1			
Cardiac	1			
Obstruction (+ entero-enterostomy)	2			
Evisceration	1			
Poor Late Results	(24)	(4)		(1)
Pain, vomiting, or both	16	3		
Recurrence of ulcer	4			
Recurrent hemorrhages	2			
Marginal ulcer	1			
Gastrocolic fistula	1			
Obstruction		1		1

Although they play no part in this study, it may be interesting to note in passing that eight cases of acute perforation of duodenal ulcer received a gastro-enterostomy in addition to ulcer closure. Three of these died, a mortality of 37 per cent, and we have abandoned the procedure except as a matter of inescapable necessity.

The attitude toward gastric ulcer, even from the earliest days, has been marked by a desire on the part of the surgeon to rid his patient of a menacing pathology. Whether one believes, with Lahey,¹⁰ that cancer does not supervene in more than 5 to 6 per cent of gastric ulcer, or with Hinton,¹¹ who expresses doubt whether this ever occurs at all, or whether one is uncertain on the question and takes into consideration only the dangers of hemorrhage and perforation, one must agree with most surgeons that the unhealing, intractable stomach ulcer is better out than in. As in the cases of duodenal ulcer in this series, most of the gastro-enterostomies, with or without ulcer excision, were performed in the earlier years. But two gastro-enterostomies have been performed for chronic gastric ulcer since 1931. The Polya operations are scattered pretty well throughout the series in point of time, but distinctly outnumber the gastro-enterostomies during more recent years.

The results of these operations for ulcer of the stomach are shown in Tables III and IV. The relatively high mortality among the simple gastro-

enterostomy cases is in some degree attributable to the fact that this operation was more likely to be performed, as a less severe procedure, on the more debilitated patients. Undoubtedly, though, whatever the operation, the gastric ulcer patient appears to be a poorer risk from the surgeon's point of view. Gastro-enterostomy with local ulcer excision or cauterization, perhaps because applicable to the smaller and simpler ulcerations, gave the best early results in this group.

TABLE III

CHRONIC GASTRIC ULCER

Operation	Number	Good Results		Poor Results	Died	Percentage
		Early	Late			
Gastro-enterostomy	17	4	5	3	5	30
Gastro-enterostomy + local excision or cauterization	15	6	7	2	0	
Polya	21	5	12	1	3	14
Billroth I	2		2		0	
Billroth II	1		1		0	
Sleeve resection	1		1		0	

TABLE IV

CHRONIC GASTRIC ULCER

	Gastro-enterostomy (17)	Gastro-enterostomy + Excision or Cautery (15)	Polya (21)
Early Complications (Survived)			
Obstruction		1	1
Hemorrhage	2		
Causes of Death	(5)	(0)	(3)
Cardiac	1		
Shock	1		
Evisceration	2		
Uremia	1		
Peritonitis			2
Pneumonia			1
Poor Late Results	(3)	(2)	(1)
Pain	2	1	1
Developed carcinoma	1		
Recurrence of ulcer		1	

These tables, representing the treatment accorded to primary ulcerations of the stomach and duodenum, do not by any means tell the whole story. There is another group of cases representing late results and complications of previous ulcer surgery that is very significant. These cases, shown in Table V, have been the most difficult to deal with technically and have often presented problems of some complexity. They are interesting as showing what may, and frequently does happen to the patient upon whom some surgeon has previously exercised his best judgment and skill. It is the occurrence of these cases that it should be our particular aim

TABLE V
OPERATIONS FOR OTHER THAN PRIMARY ULCER

Late Complication of	COMPLICATIONS					TREATMENT					RESULTS			
	Recur- rence of Ulcer	Hemor- rha- ge	Mar- ginal Ulcer	Gastro- colic Fistula	Obstruc- tion of Stoma	Bilroth II	Polya	Gastro- enterostomy	Horsley	Take-down of Gastro- enterostomy	Suture of Per- foration	Good	Poor	Died
Gastro-enterostomy (14 cases)	2	2	7*	2 [§]	1	4	5	1†		2	2	8	5	1§
Suture of perforation—gastric (2 cases)	2							2				1	1	
Suture of perforation—duodenal (2 cases)	2						1		1			2		
Pyloroplasty (3 cases)	1		1†		1		1	1			1	3		
Bilroth I (2 cases)	1				1			2				1	1	
Polya (1 case)			1†								1		1	

* Two acute perforations
† Acute perforation
‡ Anterior, plus entero-enterostomy
§ Gastrocolic fistula, peritonitis

to prevent. The cases in this group have come to us from various sources, some from our own services. It is of interest to note that, with the exception of one Polya resection that suffered an acute perforation of a gastrojejunal ulcer at the end of six months, all the other complications occurred from one to 18 years after the original operation. Of the 14 complications following gastro-enterostomy, five occurred more than ten years after the primary operation. It is obviously unfair to evaluate the results of any of these gastric operations upon the basis of "five-year cures," or in fact upon any arbitrary time standard. Neither is it fair, since in any series so many cases are lost track of in the course of time, to consider all cases as cured who fail to return even after several years of follow-up.

It is, among other things, this difficulty in evaluating late-results that has led to such differences of opinion as to the proper choice of operation for chronic peptic ulcer. To gain some idea of the scope of this controversy, a consideration of Fogelson's¹² exhaustive review of recent literature is recommended. The comments of authorities on both sides of the question of radical surgery as opposed to conservative operations are impressive, but confusing. The present contribution, with its small number of cases, cannot hope to add much to what has been said and written by so many. Yet the experience that these cases represent has been important to us, and has led to a certain viewpoint which may be briefly expressed.

As to chronic duodenal ulcer, we now feel that once the resources of medical treatment have been exhausted, without lasting benefit to the patient, he should be operated upon. This naturally brings to surgery a group of cases suffering from scarred or sclerosing ulcers, ulcers penetrating the head of the pancreas, ulcers invading blood vessels (usually in the pancreas), and ulcers which have caused duodenal or pyloric stenosis. For such ulcers, especially in the younger age group with high gastric acidity, we believe that extirpation of the ulcer and removal of the most actively acid-secreting portion of the stomach is best. In this, we find ourselves in agreement with Balfour,¹³ who feels that in such cases, where motor and secretory activity are marked, the recurrence rate of ulcer is likely to be high. While resection, of the Billroth II or Polya type, he finds, may result in subsequent jejunal ulcer, this is less likely to occur than in gastro-enterostomy, and recommends, as do Ochsner⁹ and Engel¹⁴ that such a resection should be performed quite high in the stomach. Page and Rankin¹⁵ continue to support gastro-enterostomy as satisfactorily altering the mechanism and chemistry of the stomach. Snell¹⁶ claims a 30 to 50 per cent reduction of acidity following this operation. Engel¹⁴ feels that the effects on neutralization and on pepsin action by this means are greatly overrated. Ochsner⁹ believes that the employment of a gastro-enterostomy in such actively secreting stomachs, subjecting a susceptible part of the intestine to the action of acid chyme, is an unwise procedure, and that it favors the development of marginal or jejunal ulcers.

While we have insufficient data in our own series to indicate the late results of our own resections, we have been impressed by the satisfactory early

recovery of those patients, and by the fact that the mortality has been low, even as compared with gastro-enterostomy (no death in ten cases of resection, 6 per cent in 148 patients with gastro-enterostomy) The late, unfortunate complications of previous gastro-enterostomies seen in this series have no doubt influenced us as well, and have led to the feeling that, in this particular type of case, resection gives the better hope of ultimate success The first surgical operation performed upon a patient presents the best opportunity for securing a lasting good result The technical difficulties and dangers of secondary operations are too great for comfort

In the class of patients with very high acidity, we believe that partial resections of the stomach have certain advantages over the pyloroplastic or gastro-duodenal anastomosis type of operation (Finney, Judd, Holsley, Billroth I) There is considerable question, as voiced by Balfour,¹³ whether these operations in the pyloric area adequately control the factors precipitating ulceration They are of distinct value, however, in cases of long standing pyloric narrowing, where, as in older patients particularly, the acid secreting activity of the stomach is appreciably diminished and where prolonged distention of the stomach with stenosis and gastritis has produced a certain atrophy of the mucosa They have the distinct advantage, too, in older patients, of being primarily safer than the more radical procedures The same may be said as regards the applicability of gastro-enterostomy We would reserve this operation, in duodenal ulcer, for cases of stenosis with subnormal gastric acid values In these, its results have been most satisfactory

In the performance of resections for duodenal ulcer, it is ideal to remove the ulcerated area at the same time This, however, owing to marked involvement of the pancreas or to a somewhat debilitated condition of the patient (as in bleeding ulcer, for instance), may not always be expedient, as it may involve too grave a risk Then, as Lahey¹⁰ recommends, the ulcer may be left *in situ*, though now protected from further chyme irritation, with very good prospect of a satisfactory result Occasionally, recurrence will be seen, but this must be weighed against the risk involved in resection for the particular case In the cases of repeated, bleeding duodenal ulcer, it has been our practice not to interfere surgically until the hemorrhage has been controlled and the patient restored, as far as possible, to good condition The mortality from primary hemorrhage, we believe, is not so great as would be the case were surgery employed in the instance of dangerous, apparently uncontrolled, bleeding Even though we are performing more resections than gastro-enterostomies, our views on the surgical treatment of chronic duodenal ulcer still agree definitely with those of the less radical school Rankin,⁸ one of the chief proponents of conservative stomach surgery, says, as did Peck, that the cases of recurrent hemorrhage, of ulcers penetrating the head of the pancreas, and of ulcers which are intractable owing to induration, infiltration, and presence of excessive callous, merit resection With the method of case selection we now employ, and operating as we do, in consequence, on fewer patients, we find that such cases as he considers proper subjects for resection far exceed the

10 per cent of the whole surgical group which is his estimate of their relative occurrence

In the field of chronic gastric ulcers, there is, as has been indicated, but little question as to the desirability of the extirpation of the lesion. Here, the same criteria as to operability are recognized as in the case of the duodenal lesion, but always with the question in the surgeon's mind as to the possibility of malignancy. It is this question, particularly, that leads to the more radical viewpoint in the handling of these lesions. While the local excision or cautery puncture of the smaller ulcer, together with gastro-enterostomy, may serve to secure and maintain a cure in many cases, we are inclined to favor resection, where the risk is not too great for the patient, for two reasons. First, by removing the vulnerable area of the stomach and by altering more profoundly the stomach chemistry, it makes recurrence of ulceration less likely. Second, it distinctly diminishes the probability of advancing malignancy should there be any suspicion of cancer. Balfour¹¹ reports 6 per cent of cancers developing after gastro-enterostomy in cases where the ulcer was not suitable for removal. It has been amply demonstrated that it is by no means always possible to differentiate cancer from ulcer at operation, and even in the laboratory this distinction sometimes presents difficulties. Again, however, the risk to the individual patient must be carefully weighed, and the decision as to type of operation determined primarily on that basis. It will be recalled that, in the present small series of gastric ulcers, we had five deaths after simple gastro-enterostomy in 17 cases, three deaths in 21 Polyas, and none in 15 gastro-enterostomies with local excision, but one of the latter group (not included in the table because review of the original sections showed the pathology) died later of cancer of the stomach.

The large ulcers, associated, as they often are, with considerable areas of surrounding gastritis and frequently with multiple ulcerations, do not lend themselves well to local excisions. Not only are such excisions and sleeve resections open to the same objections as is the excision of smaller ulcers, but they present, in addition, fully as great technical difficulty and risk as a well-planned resection. Moreover, they are likely to leave a deformed and often physiologically unsatisfactory stomach. In these large ulcers, therefore, resection is preferred where the patient's condition will permit. On this matter of choice of operation, Balfour¹² says "When partial gastrectomy can be performed with little more risk than excision and gastro-enterostomy, it can never be condemned for gastric ulcer." Hinton¹¹ thinks the operative mortality is too high to warrant resection as a protection against cancer.

In the difficult and complex problems presented by the patient who suffers from recurrence of duodenal ulcer, from jejunal or marginal ulcer, or from stenosis of the stoma following a lesser type of operation, resection remains usually the only recourse. These secondary operations involve considerable technical difficulty and are accompanied by a definitely increased hazard. While it must be recognized that the mere taking down of a gastro-enterostomy, or the adding of a fresh one to relieve obstruction is by no means certain

to result in permanent benefit, the patient's individual ability to withstand a proposed resection must be taken seriously into account in choosing the operation to be performed, and may lead one to choose the lesser alternative.

The question of the patient's condition and ability to withstand the operation that may be planned for him is of paramount importance. The success of these various operative procedures will depend upon the judgment with which we apply them, not to the lesion, but to the patient. In this regard, the prolonged period of medical care that precedes operation has proven of great help to us in gaining, from the patient's physician, a clear idea of his physical status. The "court" that sits upon his case brings further judgment to bear upon this point, and tends to curb any undue individual enthusiasm for some particular operative method. But whatever program is laid down for the operation must be subject to variation, modification, or abandonment by the surgeon if the conditions found at operation warrant. An inflexible attitude of adherence to a set plan is never more to be deplored than when applied to a problem of gastric surgery.

A further safeguard for the patient lies in his preparation for the operation. It is our plan, when all that can be done for him in the way of elimination of foci of infection and rectification of constitutional defects has been accomplished during his medical regimen, to give the patient a rather intensive preoperative preparation. Where no contraindication exists, his stomach is lavaged once or twice daily for several days to relieve inflammation, restore tone, and overcome retention if it exists. During the three or four days preceding operation, he is given daily two infusions of 1,000 cc of glucose, 5 per cent, in normal saline, to build up a good fluid and glycogen reserve. If his blood count is subnormal, he receives one or more transfusions before operation. As a regular measure of postoperative care, he receives a transfusion upon leaving the table, and during the succeeding days, until he takes his fluids in adequate quantity by mouth, his water balance is kept up with sufficient infusions for the purpose, supplemented by tap water by rectum. Once recovered, experience has amply demonstrated the necessity for prolonged, perhaps permanent, observation and control of these patients with respect to their habits, activity, and diet.

We are encouraged in the pursuit of the policies and practices above outlined by the early results in the present group of cases. The 14 year period covered by this report shows a mortality in Polya and Billroth II resections, for all types of primary peptic ulcer, of 9.3 per cent. This compares favorably with the 8.5 per cent mortality of gastro-enterostomies during the same period, when one considers the 16 per cent of recorded late poor results with gastro-enterostomy, as against the 3 per cent of poor results with resection. These figures, too, do not take into account the cases of secondary complications shown in Table V.

We are yet far from content with the present status of ulcer therapy. We recognize, as Ochsner⁹ enumerates them, the precipitating factors which lead to ulcer formation or promote its recurrence, namely, hypersecretion, hyper-

acidity, focal infections, reflex pylorospasm, and gastric trauma. In the control of these, we have progressed a little way. But the underlying factors, the constitutional, predisposing, individual causes of susceptibility to this disease still elude us. The search for the true etiology of peptic ulcer must continue to be pursued vigorously. Whether we shall find the answer in the field of the autonomic nervous system, or of the endocrine glands, in the manifestations of toxicity or of infection, we are, as Adams¹⁷ points out in reviewing the various hypotheses, still in the dark. For the present, we must continue to treat the complications of this disease according to our best surgical judgment, but when the true key is found, the surgeon may thankfully lay down his scalpel and relegate the control of peptic ulcer to the competent hands of his medical confieres.

SUMMARY

(1) Our experience at the Roosevelt Hospital is recorded to show how we have come to consider chronic peptic ulcer as essentially a disease for medical treatment, and how we have reached the belief that the surgical treatment of ulcer is essentially the treatment of its complications, rather than of the disease itself.

(2) We are treating to-day, by surgical intervention, far fewer cases of gastric and duodenal ulcer than was formerly our practice.

(3) Before being submitted to surgery, all cases must have had the benefit of a carefully controlled medical management.

(4) The decision to employ surgery in a given case rests with a "court" consisting of physician, surgeon, gastro-enterologist, and roentgenologist.

(5) The application of these principles has resulted in bringing to surgery a relatively larger number of patients in whom the more radical types of operation are required.

(6) The type of operation to be employed in each case is determined by certain guiding principles:

(a) It must be of such a nature that the particular patient can tolerate and survive it.

(b) It should aim not only at alleviation of symptoms, but should give freedom from likelihood of recurrence or of complications, both early and late.

(c) The ideal procedure having been determined, it should be abandoned or modified if the condition found at operation warrants.

(7) Careful preoperative preparation of each patient is required.

(8) Careful postoperative management is essential. The use of transfusions after stomach operations has become virtually a matter of routine.

(9) Careful late postoperative management is essential. The factors believed to have been involved in the original production of the ulcer must continue to be eliminated. For this purpose, a consistent and prolonged follow-up is requisite.

(10) A comparison of mortality and results encourages us in the continued employment of the practices outlined

(11) We continue, hopefully, to seek the true etiology of ulcerations of the stomach and duodenum in order that our treatment of them may become less symptomatic and more rational

(12) We believe that future success in the treatment of peptic ulcer lies in the direction of its prevention or early control, through a better understanding of its causes and nature, rather than in that of more brilliant, daring, and technically improved surgical attack upon the stomach and duodenum

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GASTRO-ENTEROSTOMY¹

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DURING my early surgical training I was taught that acute ulcers of the stomach and duodenum were medical conditions and did not require operation unless repeated attempts at cure had failed or complications developed which made surgical interference advisable or necessary

The next step in my surgical education was the teaching that the simplest operation which will relieve the patient's symptoms, cure the condition, and has the lowest mortality, is the operation of choice. As the result of this teaching and my own observations I have for a long time been under the impression that gastro-enterostomy is a very satisfactory procedure if applied in the cases in which it is indicated, and if performed with all the attention to detail which it requires. Consequently I have viewed with misgivings the campaign against this operation and in favor of routine radical procedures

It has become, and is my feeling today that such teaching is not in the best interest of the patient. No harm will probably be done in the larger surgical centers, because the members of their staffs have sufficient material to make their own observations and form their own opinions. But much harm may be done by inducing surgeons who infrequently have occasion to perform an operation on the stomach to give up a well tried, and on the whole satisfactory, operation which carries with it a low mortality, for a radical procedure with its resultant higher mortality

In order to determine whether my impressions were erroneous I decided to examine the value of gastro-enterostomy on the basis of my own material as well as that of others. In addition to my personal cases I have, therefore, made a study of the more recent literature

Gastro-enterostomy was first performed by Wolfler¹ at Billroth's Clinic, in 1881. The patient was a man with an inoperable cancer of the pyloric end of the stomach. Rather than close the abdomen without attempting to give relief, Wolfler decided to make a new opening between the anterior wall of the stomach and a loop of jejunum, and called the operation "gastro-enterostomie." The patient recovered from the operation. Soon thereafter his chief, Prof. Theodor Billroth, performed the same operation on a similar case. This patient succumbed as the result of persistent vomiting. An autopsy showed that spur-formation, due to prolapse of the intestinal wall opposite the stoma, had divided it into two openings, the larger one communicating with the proximal, and only a very small one with the descending loop. Stomach contents would thus regurgitate easily into the ascending loop and distend it until

¹ Read before the New York Surgical Society, March 9, 1938. Submitted for publication February 23, 1938.

the pressure projected it back into the stomach, while almost none passed into the lower intestine. The dangers of anterior gastro-enterostomy by a vicious circle were, therefore, recognized early. During the following years the principles of the operation were applied to nonmalignant pyloric obstructions, notably by Rydiger,² who, in 1884, operated upon an emaciated boy, age 20, with an obstruction due to a stenosing ulcer, and obtained a successful result.

In order to try to avoid the difficulties of a vicious circle so frequently following a long loop anterior gastro-enterostomy von Hacker³ conceived the idea of performing a retrocolic, posterior gastro-enterostomy. With slight modifications or additions this has remained the operation of choice in those cases in which no technical obstacles to its performance are encountered.

It is apparent that the operation was conceived as a side-tracking procedure for the relief of pyloric obstruction, whether malignant or benign. The results of the operation in this type of case were so very gratifying, that the thought suggested itself to apply the same principle to ulcers not associated with mechanical obstruction. It was hoped that by putting the ulcer at rest by an exclusion operation, healing might result. The unexpectedly good results which followed this procedure led to investigations as to the cause of the beneficial effect.

Its action in mechanical obstruction is easy to understand, because there it acts actually as a side-tracking operation and brings relief by drainage. Its action in ulcer cases without obstruction is not so easily explained. If a certain amount of pylorospasm is present as the result of hyperacidity and irritation from a near or more distant ulcer the same explanation may suffice. However, if there is no obstruction at all the pylorus remains patent after gastro-enterostomy and food may, and often does, leave the stomach by the two openings. The opinion then gained ground that the influx of duodenal contents through the new stoma alkalizes the stomach contents and, thereby, induces a beneficial healing action on the ulcer. However, this question still remains a controversial one. Nevertheless, it is true that ulcer patients have been relieved by the operation in a high percentage of cases and one has to assume that the altered physiology of the stomach in some way exerts a beneficial influence. It is readily conceded that there are a certain percentage of ulcer patients who are not relieved or cured by gastro-enterostomy, or in whom a new group of symptoms due to secondary ulcer formation at or near the stoma is initiated. These two reasons, failure to cure the ulcer and an alleged high frequency of secondary gastrojejunal or jejunal ulcers, have led some surgeons to the conclusion that radical surgery, meaning by that partial or subtotal resection of the stomach, is indicated for the cure of both duodenal and gastric ulcers. Advocates of radical surgery as a routine procedure claim an incidence of 10 to 20, and even more, per cent of jejunal ulcers following simple gastro-enterostomy. This is at variance with the experience of most surgeons, and most of the large clinics of the country, which report only 3 to 4 per cent of such ulcers.

Nevertheless, the campaign in favor of radical surgery has succeeded in

discrediting gastro-enterostomy to such an extent that many surgeons are disinclined to advocate it

It is, therefore, timely to determine whether it is justified to abandon an operation which, through the years, has given such satisfactory results, for a more radical procedure with its attendant higher mortality, and a doubtful guarantee that it will not be followed by the very sequelae for the avoidance of which it was instituted

We may quickly pass over the question of gastro-enterostomy for carcinoma of the stomach. It is at most a palliative measure, and is used only in those patients in whom a radical operation cannot be performed because of technical difficulties or because the general condition of the patient does not permit. In such individuals the mortality is, therefore, expected to be high. When technically possible to be performed without undue tension on the suture lines, the results are good, and usually insures the patient relief of symptoms and several months of comfortable life.

The real interest in the operation of gastro-enterostomy centers about its use in cases of gastric and duodenal ulcer, as well as in the complications or sequelae of these conditions, namely, hemorrhage, local perforation and scar contracture with consequent pyloric obstruction.

All surgeons agree that the problems connected with the surgical treatment of gastric ulcer differ considerably from those associated with duodenal ulcer, and that they should, therefore, be considered separately.

In duodenal ulcer a side-tracking operation by gastro-enterostomy is possible and the ulcer may be put completely at rest, whereas, in gastric cases this is usually not the case. Only in those ulcers situated near the pylorus and producing some degree of spasm or stenosis may one reasonably expect such a result. Cautery destruction or excision of ulcers has not been as successful as was hoped for. There is in addition a tendency to cancerous degeneration of gastric ulcers variously estimated at from 10 to 20 per cent. This, coupled with the general experience that conservative treatment in gastric ulcer is less satisfactory than in duodenal ulcer, has induced most surgeons to advocate, and perform, partial gastrectomy in those cases which have not responded to medical treatment.

We fully agree with this view and have for years performed this operation as a method of choice. The fact that the duodenum is not involved, and permits safe closure of the stump, usually makes it less dangerous than a resection for duodenal ulcer. Unless the ulcer has perforated and is extensively adherent to the pancreas, there is no unusual risk connected with the operation in a patient in fair general condition.

While conceding that resection is the treatment of choice, gastro-enterostomy, nevertheless, has a definite, though limited, place in the treatment of gastric ulcer. This is particularly true of the large hypertrophic ulcers of the pylorus and prepyloric region, which not infrequently simulate inoperable carcinoma. It is also of value in ulcers near the pyloric end with inflammatory reaction and extensive adhesions, and in some of the ulcers situated high on

the lesser curvature Here they are inaccessible, and attempt at removal by resection dangerous Closure so high up is difficult and fatal leakage may result Relief of symptoms or cure may be obtained after gastro-enterostomy, and is best explained by subsidence of pylorospasm with better drainage, as well as by alkalization of the stomach contents

The question of the surgical treatment of duodenal ulcer is the one we are chiefly interested in at this time because it is this group in which we are asked by the advocates of routine radical operation to substitute gastric resection for gastro-enterostomy

The original communications on this subject by Habeier,⁴ and other German authors, as well as those by its American advocates, stress failure to cure duodenal ulcer by gastro-enterostomy, as well as the frequency of postoperative marginal or jejunal ulcers as reasons for abandoning gastro-enterostomy and substituting therefore partial or subtotal gastrectomy A A Berg⁵ bases his plan of treatment on the necessity of removing the three factors which he holds responsible for the formation and development of an ulcer, namely, chronic specific gastritis, the presence of free hydrochloric acid in the stomach, and the presence of a secondary infection in the stomach or duodenum The procedure that will most nearly accomplish this is partial or subtotal gastrectomy On the basis of a large material he builds up a very good case in favor of early radical surgery, and describes an operative procedure which, in his hands, has been followed by a very low operative mortality and excellent late results

Lewisohn,⁶ in an analysis of 68 cases of gastro-enterostomy with or without pyloric occlusion, found a perfect result was obtained in 47 per cent, a fair result in 19 per cent, and the remaining 34 per cent had gastrojejunal ulceration He explains this unusually high incidence on the basis of careful personal reexamination of the patients, and evidently believes other surgeons would find a similarly high incidence if they followed their cases more carefully He rejects the possibility of faulty technic as a factor, but definitely holds persistent hyperacidity in the gastro-enterostomy cases responsible for the continuation or aggravation of symptoms It is his firm belief that the important factor in the prevention of subsequent gastrojejunal ulcers is anacidity, not the technic of the operation, and that such an anacidity is best obtained by subtotal gastrectomy Several other surgeons share this view and are advocating radical procedures as a routine, while another group are performing resections on carefully selected cases only There is a great deal of experimental evidence to support the attitude of these surgeons, though many reports contradict one another and leave one in somewhat of a state of confusion

Recent observations by DeBakey⁷ on dogs upon which a von Eiselsberg exclusion was performed, in conjunction with an anterior gastro-enterostomy, showed 50 per cent jejunal ulcers after operation The ulcer always appeared in the efferent loop where the acid neutralizing power of the duodenal contents had been largely lost He concludes that the jejunal mucosa is func-

tionally unable to receive acid gastric chyme and that inadequate neutralizing power of the duodenal secretion apparently plays an important rôle in ulcer production. In order to prove the protective value of the various components, he diverted the pancreatic juice from the duodenal contents, so that the only protective agents remaining were bile and succus entericus. After such a procedure ulcers developed in 70 per cent of cases. If he also diverted the bile, ulcer developed in 90 per cent of cases, and not only in the efferent loop but also at the anastomotic line and opposite the stoma in the jejunum. He holds bile to be the most significant protective factor. The author further stresses the importance of foreign body such as suture material as a possible cause of ulcer and quotes a number of authors in support of this view. However, he also cites several cases in which suture material was found at the stoma without ulcer formation.

In a more recent paper on the physiology of peptic ulcer, DeBaKey emphasizes the fact that no single factor can be held responsible for peptic ulceration in general, which is a viewpoint held by most thoughtful observers.

Against these views of the proponents of routine radical surgery there are any number of articles based upon clinical observation citing excellent results following gastro-enterostomy. There are also numerous laboratory studies which show the beneficial effects of the operation upon the acidity of the stomach.

Heuer,⁸ in a recent paper on the choice of operations in the treatment of peptic ulcer, mentions three methods of operative procedure for duodenal ulcer. Local excision of the ulcer combined with some form of pyloroplasty, a simple gastro-enterostomy, and pylorectomy or partial gastric resection. Each type is indicated in certain cases. He collected 1,559 gastro-enterostomies for duodenal ulcer from the recent literature, which showed a general mortality of 6.8 per cent. The late results showed 85 to 92 per cent satisfactory relief from symptoms in American clinics. Gastrojejunal ulcer as a late complication was found in about 3 per cent of cases in the experience of 17 authors from various countries. A study of the results of eight authors showed jejunal ulcer following partial gastrectomy in 19 per cent of cases.

Judd and Hazeltine,⁹ after a comprehensive review of a large series of excisions for duodenal ulcer, cite two reasons why the operation of excision of ulcer of the duodenum has not gained rapidly in popularity. (1) That the results of gastro-enterostomy when performed for this condition have usually been satisfactory, and (2) unless the first portion of the duodenum is free and mobile, excision of the ulcer may be very difficult. Unless it is possible to excise the ulcer with less risk and better results than attend gastro-enterostomy, there is no occasion for this operation. They conclude that gastro-enterostomy will probably remain the popular operation for duodenal ulcer. It is satisfactory in all cases except in those in which secondary ulcers develop, hemorrhage occurs, or bleeding may continue.

St John,¹⁰ in a comparison of follow-up statistics between 119 cases of gastro-enterostomy and 76 cases of partial gastrectomy, reports a mortality of

15.1 per cent in the former and 19.6 per cent in the latter. Of the gastro-enterostomy cases there were 92.8 per cent symptom free or improved, and of the gastrectomy cases, 96.8 per cent were symptom free or improved. The unusually high postoperative mortality is due to pulmonary complications. The author reports marginal ulcer in 6.9 per cent of the gastro-enterostomies, and in 3.6 per cent of the resections.

Balfour¹¹ presents a very complete analysis of 500 cases of gastro-enterostomy for duodenal ulcer which had been observed after a minimum of five years after operation. The operation was performed in most instances in chronic cases. Eighty-seven per cent obtained relief, which they had been unable to obtain by any other means, and in 69 per cent it was so complete that the patient was not conscious of having a stomach. The operative mortality was 1.8 per cent. In no case did perforation of the duodenal ulcer occur after gastro-enterostomy had been performed, which makes him feel that this operation, apparently, affords absolute protection against this serious complication. Likewise in none of the cases of this series did obstruction of the pylorus develop subsequent to operation. However, it seemed more difficult to secure permanent protection against hemorrhage, for 45 of the 500 patients, or 9 per cent, had one or more hemorrhages, but only one died as the result of it. The protection afforded by gastro-enterostomy against the formation of a secondary chronic ulcer is approximately 96 per cent, for in only 3.26 per cent, gastrojejunal or jejunal ulcer occurred in a period of ten years or more after operation.

Balfour also studied 100 cases of gastro-enterostomy performed for gastric ulcer. Although he believes in removing the lesion if reasonably possible, he is convinced that gastro-enterostomy alone is the operation of choice in those cases in which the size of the lesion, its situation, or the age or condition of the patient makes its removal a difficult or hazardous procedure. The operative mortality in this group was 3 per cent. Seventy-nine per cent of the patients, five years or more after operation, were relieved, with complete relief being obtained in 60 per cent. No gastrojejunal or jejunal ulcer developed.

He feels that gastro-enterostomy has its greatest application in cases of chronic duodenal ulcer in which there is impairment of motor function and in which the acid values are not unusually high. Since impaired motor function usually occurs late in the development of duodenal ulcer, it is in the most chronic cases that gastro-enterostomy is so effective. In a more recent paper on peptic ulcer and its surgical treatment by conservative measures, Balfour repeats that he believes gastro-enterostomy to be the most useful of the different procedures which may be employed. He states that if the operation could be confined to the more chronic cases there would be no criticism of it, but the very fact that it did bring about such spectacular results in this group led to its employment in cases in which there was no impairment of motor function and in cases in which symptoms were of short duration. It is probably for this reason that so much criticism of the operation has arisen, because it is in

this group that disappointing results are most likely to occur. He further states that when the indications for gastro-enterostomy are understood and carefully observed, the results are strikingly similar. Between 80 and 90 per cent of patients have obtained satisfactory results following gastro-enterostomy, and there have been only 3 to 4 per cent with subsequent jejunal ulcer formation.

Walters¹² disposes of the arguments in favor of routine radical surgery, particularly with regard to the frequency of gastrojejunal ulcers following gastro-enterostomy, by stating that he has rarely seen them, not more frequently than after gastric resection, and again, relative to the statement that associated gastritis is a cause of duodenal ulcer, as well as of recurrence of symptoms after gastro-enterostomy, by stating that gastritis has rarely been found in the specimens removed by them.

He also quotes from a collective investigation by the British Medical Association, in 1928, into the after-history of gastro-enterostomy cases operated upon during 1920 to 1924. According to this report gastrojejunal ulcer occurred in 28 per cent of 744 cases in which gastro-enterostomy was performed for duodenal ulcer. The postoperative mortality was 5 per cent. The results of the operation were satisfactory in about 90 per cent of the cases.

His paper further deals with the question of tissue resistance and tissue susceptibility, particularly to hydrochloric acid, and makes a comparison between the relative achlorhydria obtained in groups of cases treated surgically by different methods. He concludes that tissue resistance and tissue susceptibility to hydrochloric acid, and their measurement, are the factors upon which successful treatment of duodenal ulcer depends regardless of the surgical procedure employed, for, if tissue resistance to hydrochloric acid is satisfactory, ulceration will not recur, whereas, when tissues are susceptible to the hydrochloric acid of the gastric secretion, ulcer may recur, if free hydrochloric acid persists in sufficient degree, regardless of the surgical procedure employed. In his opinion gastric resection has a place in the treatment of certain of the hemorrhagic duodenal ulcers as well as in the treatment of recurring duodenal ulcer and of gastrojejunal ulceration, it is also applicable in the treatment of patients whose tissue has lowered resistance to the hydrochloric acid in gastric secretion.

In 1924, Charles H. Peck¹³ discussed the status of the surgical treatment of chronic duodenal and gastric ulcer at that time, and strongly favored gastro-enterostomy. He contended that it served its purpose as well in those patients without obstruction as those with it. In a total of 196 cases of chronic duodenal ulcer there was a mortality of 8 per cent, and a favorable result, which he considered to mean a lasting clinical cure, in from 80 to 90 per cent. Only one case came to secondary operation for gastrojejunal ulcer, and another for a rigid, painful stoma, while in two other cases there were symptoms suggestive of secondary ulceration, but which were not definitely proved. Peck stressed the word "chronic" in dealing with the subject of the surgical

treatment of ulcer, and he was a firm believer in adequate medical treatment before advising operation

In 1933, Klein, Aschner and Crohn¹⁴ published a report of a study in the pre- and postoperative gastric secretion in 108 cases in which a subtotal gastrectomy had been performed on the service of Dr A A Berg at Mt Sinai Hospital (Table I)

TABLE I
DEGREE OF PRE- AND POSTOPERATIVE ACIDITY (*Klein, Aschner and Crohn*¹⁴)

<i>Preoperative Acidity</i>		
Number of Cases	Degree of Acidity	Percentage
38 gastric ulcer cases	Normal or subnormal	50
	Hyperacidity	50
210 duodenal ulcer cases	Normal or subnormal	10
	Hyperacidity	90
<i>Postoperative Acidity (early)</i>		
Number of Cases	Degree of Acidity	Percentage
35 gastric ulcer cases	Promptly became anacid	77
	Were normal or subnormal	14
	Remained hyperacid	9
197 duodenal ulcer cases	Showed anacidity	38
	Were normal or subnormal	48
	Remained hyperacid	14

In the 108 cases cited above, with adequate follow-up Rehfuß tests over periods of one to eight years, 56 per cent either remained anacid or became anacid while under observation. In one of the gastric ulcer cases which became anacid, recurrence developed, while there were nine jejunal ulcers in the group of duodenal ulcer cases which had not become anacid after gastric resection

Such a finding materially weakens the argument in favor of subtotal gastrectomy, for, though it is definitely shown that anacidity follows resection in a large percentage of duodenal ulcers, the occurrence of jejunal ulcer in those cases in which free hydrochloric acid persists is higher than has been reported from most clinics following gastro-enterostomy

Our own experience with primary gastro-enterostomy has been gained from 84 cases. In 12 of these the operation was performed for inoperable carcinoma. They may, therefore, be eliminated from our discussion, leaving 72 cases for consideration. Of these 72 cases, three were not originally operated upon by me, but came under my care for some complication, one with a gastrojejunal fistula, and two with symptoms of recurrence. In one of these, twisting of the intestine with adhesions at the site of anastomosis was found, in the other, a ventral hernia, but a normal gastro-enterostomy. Both of these were relieved. There were three cases in the group which had had a previous conservative operation for ulcer: one a closure for perforation, one a pyloroplasty and the third excision of an ulcer. All three had recurrent symptoms with stenosis and were relieved by gastro-enterostomy (Table II)

TABLE II
ANALYSIS OF INDICATIONS FOR WHICH GASTRO-ENTEROSTOMY
WAS PERFORMED IN 72 CASES

Indications	Number of Cases
Chiefly ulcer symptoms	39
Chiefly symptoms of obstruction	17
Combined symptoms of ulcer and obstruction	16
Total	72

Well over half the patients were over 40 years of age (Table III)

TABLE III

AGE INCIDENCE

20-30 Years	30-40 Years	40-50 Years	50-60 Years	60-70 Years
18	13	11	23	7

Complications were quite numerous. Those connected with the respiratory system were not serious and none ended fatally. One developed a lung abscess, apparently due to aspiration, and was operated upon subsequently, successfully. In two patients a cardiac infarct was diagnosed. There were two patients with suppurative parotitis, one of whom had to be operated upon.

The complications connected directly with the operation consisted of hemorrhage, vicious circle, and evisceration. In the first patient upon whom I performed a gastro-enterostomy, I gained experience with all three of these complications. Immediately after operation he began to vomit blood, repeatedly and in large quantity. Bleeding was controlled by gastric lavage with hot saline and instillation of dilute adrenalin solution. As the result of vomiting and straining he broke open his abdominal wall, which required secondary suture. Then he developed symptoms of vicious circle which became so severe as to necessitate reoperation. An entero-enterostomy was performed. He has since been entirely free from gastric symptoms. This is the only patient in whom I ever performed a pyloric exclusion at the same time as the gastro-enterostomy. Whether that had anything to do with the complications I do not know, but it made such an impression on me then, that I have never employed the procedure since.

There were two other patients with severe postoperative hemorrhage, one of which ended fatally, apparently due to bleeding from the ulcer. She never vomited blood, but simply became progressively more anemic without any symptoms and expired on the sixth day. There was no autopsy. The third case was a young man, age 29, who within 12 hours after operation vomited large quantities of blood. The bleeding threatened to end fatally, but was controlled by suture ligation of the bleeding points at the anastomosis.

Except in the case cited above, vicious circle did not develop in any patient. There have at times been lesser disturbances suggestive of it, but they have always adjusted themselves.

Evisceration complicated the convalescence in two cases. We are under

the impression that people with a wide epigastric angle and a rigid costal arch have unusual strain put on midline or lateral incisions, and in such cases have frequently employed a transverse incision about two fingers above the umbilicus, from the outer border of one rectus to that of the opposite one. It seems to guard against evisceration.

We have never encountered a definitely diagnosed gastrojejunal or jejunal ulcer in any of the gastro-enterostomies performed by ourselves, but have had two cases in which a suspicion of the presence of one existed. One cleared up entirely and died some 12 years later of carcinoma of the stomach. The other had secondary ulcer symptoms with bleeding and was diagnosed as probable marginal ulcer on roentgenologic examination. He is well at present. We have, however, had considerable experience with one case of secondary ulceration. The patient was admitted with the diagnosis of gastrojejunal fistula. His gastro-enterostomy had been performed at another institution ten years previously, at the age of 23, on a presumptive diagnosis of ulcer, based upon a history of stomach upsets since childhood and one attack of vomiting, which contained blood, without any test meal or roentgenologic examination being made. After correction of his gastrojejunal fistula the patient was reasonably well for six years, until he developed symptoms of ulcer with obstruction at the pylorus, which later perforated against the anterior abdominal wall and formed a large mass there. This was liberated and the perforation closed transversely. There have been no serious stomach symptoms since, but, during 1937, he was admitted with intestinal obstruction which was found to be due to carcinoma of the ascending colon and required resection.

Three of the 72 cases, or 4.1 per cent, died as the result of the operation. One was due to acute gastric dilatation with cardiac failure, apparently not recognized in time, the second case died of hemorrhage, probably from the ulcer, and the third died of a peculiar dilatation of the cecum, with necrotic ulcers and multiple perforations of its anterior wall. No adequate explanation for this condition has been found. It probably had no relation to the operation or to the lesion for which it was performed.

Most of the patients have been followed since their operation. Some of those of the younger age group, under 30 years, were operated upon many years ago. They have been difficult to follow and several have disappeared from observation. One of them, a patient with what was diagnosed as ulcer of the third portion of the duodenum, recovered completely after gastro-enterostomy, but died within two years of a cancer of the rectum. There has been a suspicion that the duodenal lesion may have been carcinoma. Another of these patients died 12 years after gastro-enterostomy of exophthalmic goiter. An autopsy showed a perfect stoma. All patients were discharged as cured or improved after operation, and remained so for the period of observation. None have returned to us for subsequent treatment but that of course does not mean that all have remained well. Several were of that nervous temperament so often encountered in young patients with ulcer symptoms and it is possible that they have subsequently developed further trouble.

Of the older age groups several have died of intercurrent disease. All others have remained well except the few who developed recurrent symptoms and are mentioned under complications. A few had symptoms of indigestion or nervousness from time to time but not enough evidence of a lesion on examination to warrant the diagnosis of recurrent ulceration. We are under the impression that there has been restitution to health in at least 90 per cent of the patients. The results with gastro-enterostomy performed on ward cases at the Lenox Hill Hospital have been similar. However, the follow-up on these cases is not sufficiently accurate to warrant their inclusion in this report.

Discussion—A study of the material submitted in this paper in favor of routine partial or subtotal gastrectomy for duodenal ulcer, as well as a consideration of recent literature not quoted here, and the comparison of these with the abstracts of papers in favor of conservative surgery as well as with the reports of our own cases make us feel that there must be some explanation for these strikingly different results and opinions.

Surgeons in favor of partial or subtotal gastrectomy have reached their conclusion on the basis of certain observations which in short are: Failure of gastro-enterostomy to cure in a large percentage of cases, failure to prevent recurrences, and failure to prevent secondary gastrojejunal or jejunal ulcers. Those who do not favor this radical procedure, or rather who see no necessity for adopting it as a routine for the usual uncomplicated case, base their opinion on the generally good results which follow gastro-enterostomy, and on the fact that they do not frequently see recurrences or gastrojejunal or jejunal ulcers.

There must be some explanation for this difference of opinion and particularly difference of recorded observations. All authors may not be thinking and speaking of the same kind of a case. Some may include a large number of acute ulcers in patients of the younger age groups in whom the results may be quite different from those in the more chronic cases with some disturbance of motor function and perhaps lower acidity values. Whether adequate preliminary medical treatment has been a factor or not may play a rôle. Then there is the question of the race of the individual, his general environment, his temperament and his diet which may all have an important bearing on the behaviour of an ulcer. Taking the extremes of reported gastrojejunal and jejunal ulcers, for instance, varying from the low of 3 to 5 per cent, and comparing them with the high of 34 per cent, reported by Lewisohn,⁶ makes one wonder: Are the proponents of conservative surgery less keen observers or are they dealing with a different type of case?

In this connection it may be of interest to call attention to a recent article by Schittenhelm¹⁵ which deals with the geometrical variation of types of lesions, and by the part played by racial factors in these differences. It is known that disease processes are vitally influenced by climate, living conditions, food, general environment, *etc.*, in the same way that infections are.

It certainly gives one food for thought when one reads that some clinics

are advocating radical stomach surgery, partly on the basis of the frequency of gastritis in association with ulcer. This is notably true of some German clinics, and the same observation has been made here. The Mayo Clinic investigated this question by sending a commission to Europe and bringing a European investigator over here, in order to study the material at their clinic. It was definitely shown that there is a decided difference in the lesions, and that associated gastritis is infrequently found at the Mayo Clinic, and can, therefore, not be advanced as an argument in favor of radical surgery.

It seems evident that the selection of cases for operation must have a very important bearing on the results. It must make a big difference whether one includes in the study very young people who had a gastro-enterostomy performed for indigestion, hyperacidity, and a suspected early ulcer which sometimes cannot be demonstrated on the operating table, and compares them with the more chronic cases in an older age group, who have a definitely diagnosed and demonstrable ulcer. I have seen operations performed for suspected duodenal ulcer and at the operation no definite lesion could be found. After careful but fruitless search it was decided to do a gastro-enterostomy anyway, in the hope that it would cure the symptoms. There is no doubt that some years ago, and especially at some clinics, gastro-enterostomy was performed without proper indications, sometimes on the presumptive diagnosis of duodenal ulcer. I believe that this is the cause for many of the poor results or late complications which are now advanced as an argument in favor of more radical surgery.

I am afraid that some surgeons are now making the mistake of advocating unnecessarily radical operations for lesions which are amenable to more conservative operative procedures. Their enthusiasm sometimes carries them to a point which in the eyes of more conservative surgeons is not justified. I have seen two resections performed for suspected duodenal ulcer, one here and one abroad, which showed no pathology when the specimen was examined.

My personal feeling is that no patient with symptoms of duodenal ulcer should be subjected to operation unless he has a definitely diagnosed lesion and unless adequate medical treatment has been tried, preferably repeatedly. I do not believe that the diagnosis of duodenal ulcer per se calls for surgery. Very young people especially, with so-called nervous indigestion, hyperacidity, and that entire group of symptoms which so frequently leads to the clinical diagnosis or at least suspicion of ulcer, should not be subjected to operation. Their symptoms are usually of a functional nature and require medical attention. I fully share the views expressed by Peck as well as by Balfour and others, that it is the chronic duodenal ulcer case, the one which has resisted medical treatment and which seems to have no further hope of relief from such treatment, which requires surgery. As shown in the cases reported, many of them have some degree of obstruction associated with the ulcer, either due to spasm, periduodenal inflammation or scar contracture. It is this class of case which furnishes such excellent results after gastro-enterostomy.

To subject such a patient with an uncomplicated duodenal ulcer to a sub-

total gastrectomy seems wrong to me. It appears unsurgical to sacrifice half or more of a normal stomach in order to remove a small ulcer of the duodenum which anatomically and physiologically is separated from it.

Even admitting that jejunal ulcer may follow gastro-enterostomy more frequently than is reported from the large American clinics, should there then not be instituted a medical regimen after gastro-enterostomy to prevent them? It is claimed that it is the acid gastric chyme which, acting on an improperly protected mucous membrane of the duodenum and jejunum, produces ulcer. It is further claimed that removal of the acid bearing area of the stomach will produce anacidity and thereby prevent jejunal ulceration. Laboratory examinations made since these claims were first advanced have shown that, though anacidity is produced in a large number of cases, hyperacidity may persist after a subtotal gastrectomy and jejunal ulcer develop just the same. This would seem to point to the advisability of abandoning partial gastrectomy as a routine procedure for the cure of uncomplicated duodenal ulcer, and to continue to employ gastro-enterostomy.

For complicated cases of duodenal ulcer, especially those with massive hemorrhages, or with excessive and persistent pain which resists medical treatment, or for recurrent symptoms after a conservative operation, radical resection may be indicated, and may be the safest way to restore a patient to health. With the advances which have been made in gastric surgery, and with the modern pre- and postoperative care, resection has become a well standardized procedure, which in the hands of any well trained surgeon yields uniformly good results with a reasonably low mortality.

Technic of Gastro-Enterostomy—In planning the operation it should always be with the mental reservation that some other procedure may have to be undertaken in order to meet the conditions found. The aim of the operation is to cure the disease and to avoid complications if possible. To keep patients in bed for a few days prior to operation is valuable in order to acclimate them and to be sure that the respiratory, circulatory and excretory systems are in order. The time may be utilized for the administration of fluids and possibly a transfusion, as well as for daily gastric lavage in those patients having obstruction.

With mouth hygiene and modern anesthesia, intrapulmonary complications should be uncommon.

The incision is planned to obtain good access, and to assure a firm, strong abdominal wall. Usually an epigastric incision, just to the left of the median line, answers the purpose, but in patients with a wide epigastric angle and a rigid costal arch, a transverse incision from the outer border of one rectus muscle to that of the other is of value. It permits good exposure, assures a firm abdominal wall without undue strain, and thereby protects against evisceration.

In the operation itself certain technical points are to be observed to guard against hemorrhage, vicious circle and possibly secondary ulceration. One should choose the most dependent part of the stomach, while it lies at rest,

for the anastomosis. By turning the omentum and the transverse colon upward, a place in the transverse mesocolon which lies directly opposite this dependent part of the stomach, and to the left of the colica media, is chosen for the opening. The loop of jejunum close to the duodenojejunal junction is now picked up the way it lies at rest. The most important thing is not to twist it, but to have it lie naturally. This will avoid angulation and possible subsequent stagnation in the loop. If the conception of the cause of jejunal ulcer is correct, namely, that it is due to the acid gastric chyme striking the jejunal mucosa which is unable to protect itself against it, then any stagnation opposite the stoma may favor such a development. Maintaining a free flow of duodenal secretions in the loop will tend to neutralize whatever hyperacid gastric content has been ejected into the jejunum.

The next most important point is to place the sutures properly. The outer row is for approximation of the serosa, and beyond stating that it should be snug there is no special attention required. The inner suture line, however, is important, in that it has to be sufficiently closely approximated to stop bleeding points and to prevent gastric juice from penetrating. For this same reason none of the mucosa should be trimmed, as is occasionally done. It is all needed to protect and cover the cut edges of the intestinal wall. A simple continuous whip-over stitch serves the purpose best. The new stoma is now fastened into the opening in the transverse mesocolon with the aid of interrupted silk sutures which attach the edges to the wall of the stomach, best just above the stoma.

I believe it to be unimportant what suture material is used or whether one uses clamps. Formerly we used silk for inner and outer suture, but during the last several years silk for the outer and chromic catgut No. 0 for the inner suture line. We use the Roosevelt clamp in all suitable cases, but occasionally perform an anastomosis without clamps.

CONCLUSIONS

Gastro-enterostomy is indicated

(1) In cancer of the pyloric end of the stomach in which radical operation is impossible on account of extensive local involvement metastases, or poor general condition. If successful, it relieves symptoms and prolongs life for a while.

(2) In all benign obstructions of the pylorus due to extensive adhesions, scar contracture from ulcer, stenosis following operations for perforation, or after unsuccessful pyloroplasties.

(3) In pyloric and duodenal ulcer after repeated attempts at medical cure have been unsuccessful.

(4) In gastric ulcers near the pylorus associated with extensive adhesions or stenosis, in which a side-tracking procedure is considered to be of value.

(5) In some gastric ulcers situated so high, or so adherent, that their removal carries with it a serious threat to life.

Gastrectomy is indicated

- (1) In all cancers, if technically possible
- (2) In gastric ulcers
 - (a) As a primary operation because conservative procedures are rarely successful and because of a tendency to cancerous degeneration
 - (b) As a secondary operation where a previous conservative operation has failed or where gastrojejunal or jejunal ulceration has developed
- (3) In duodenal ulcers
 - (a) When repeated hemorrhages, especially massive hemorrhages, have not been controlled
 - (b) After failure of conservative operations
 - (c) For intractable pain
 - (d) Possibly for gastrojejunal or jejunal ulcer

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DISCUSSION OF THE PAPERS OF DOCTORS CUTLER AND EGGERS

DISCUSSION —DR CONSTANTINE J MACGUIRE, JR (New York) had recently collected the statistics on the surgery of peptic ulcer from the First Surgical Division of Bellevue Hospital. Before reporting these, however, he emphasized that in almost all cases the guide had been the principles emphasized by Doctor Cutler in his presentation, namely, that surgery of peptic ulcer is the surgery of its complications plus impracticability. In confining surgery to such cases one necessarily has a higher mortality, particularly when the patients come to the service physically and economically at the end of their resources, as is the case at Bellevue Hospital.

Since 1920, 173 cases of duodenal ulcer exclusive of acute perforations were operated upon, as reported in the ANNALS OF SURGERY, 107, 350-358, March, 1938, by Doctor McCree. One hundred thirty-three of these cases were subjected to simple gastro-enterostomy with or without cauterization of the ulcer or pyloric exclusion. Most of them had cauterization. There were six cases operated upon as a desperate measure during massive, uncontrollable hemorrhage. These were not included in the general statistics, all died, and in Doctor MacGuire's opinion surgery has no place in the acute stage of massive hemorrhage. Seventeen cases died of various causes, giving a mortality in the gastro-enterostomy group a little under 13 per cent. Of the cases followed more than two years—namely, 97—65 were free of ulcer symptoms and 32 showed varying degrees of gastric distress. Twenty-two cases of duodenal ulcer, not including the massive hemorrhage cases, were subjected to partial gastrectomy, with seven deaths, a mortality of approximately 31 per cent. This mortality could have been lowered had there been fewer attempts to resect the duodenum, as it was probably not necessary to remove the ulcer in all cases (Table I).

Pyloroplasty of various types (Horsley, Finney, *etc*) was performed for duodenal ulcer in 14 cases. Of the 10 followed, five showed good results and five persistence of some symptoms (Table I).

Of 111 cases of gastric ulcer operated upon, 33 were subjected to gastro-enterostomy with two deaths, a mortality of 6 per cent. Of 22 cases followed, 13 showed good and nine poor results (Table I).

Excision of the gastric ulcer alone was accomplished in 10 cases, with one death. Four of the nine cases followed showed good results, and five poor. Gastrectomy was performed for nine ulcers in 66 cases, with 15 deaths, a mortality of 22 per cent. This high mortality was accounted for in the fact that the majority of these patients showed very advanced ulcers, fixed in the pancreas and sometimes in the liver. Of 45 cases followed, 44 were free of gastric symptoms (Table I).

Nineteen marginal ulcers were operated upon. In 10, the original gastro-enterostomy had been performed on the First Surgical Division of Bellevue, and in the other nine elsewhere. Fifteen of these cases were subjected to gastric resection, a rather formidable feature in these cases which all showed massive adhesions. The ulcers showed a marked tendency to penetrate the posterior wall of the transverse colon. There were three deaths, a mortality of 20 per cent. Of the 12 cases followed, 11 were completely relieved and one had a recurrence. Of the cured cases however, two were marginal ulcers at the stoma. Of the previous gastric resections, one was performed on Doctor MacGuire's service and one elsewhere. Simple excision of the stoma was undertaken in four cases with one death. Of the three cases followed all have gastric distress (Table I).

Doctor MacGuire's analysis involved 302 individuals subjected to 337

TABLE I

SYNOPSIS OF RELEVANT DATA UPON 302 PATIENTS WITH PEPTIC ULCER, SUBJECTED TO 337
OPERATIVE PROCEDURES*(First Surgical Division, Bellevue Hospital)*

DUODENAL ULCERS 173 cases		GASTRIC ULCERS 111 cases	
Gastro-Enterostomy	133	Gastro-Enterostomy	33
(With or without excision, cau- terization or pyloric exclusion)		Survivors followed-up	22
Deaths in hospital	17	Deaths	2
Survivors followed more than two years	97	Mortality	6%
Free from G I symptoms	65	Free from G I symptoms	13
Persistent G I symptoms	32	Persistent G I symptoms	9
	—		
Partial Gastrectomy	22	Excision of Ulcer	10
Deaths in hospital	7	Deaths	1
Survivors followed-up	13	Survivors followed-up	9
Free from G I symptoms	12	Free from G I symptoms	4
Persistent G I symptoms	1	Persistent G I symptoms	5
	—		
Pyloroplasty	14	Partial Gastrectomy	66
(Usually Horsley)		Deaths	15 or 22%
Deaths	0	Survivors followed-up	45
Followed-up Free from G I symptoms	5	Free of G I symptoms	44
Persistent G I symptoms	5	Persistent G I symptoms	1
	—		

MARGINAL ULCERS 19 cases

Original gastro enterostomy performed on Service in 10 cases out
of 166 gastro-enterostomies, or 6 per cent Original gastro-enteros-
tomy performed elsewhere in nine cases

Simple Excision of Stoma and Jejunal Resection	4
Deaths	1, or 25%
Survivors followed-up	2
Persistent G I symptoms	2
Partial Gastrectomy and Jejunal Resection	15
Deaths	3, or 20%
Followed-up	12
Free from G I symptoms	11
Persistent G I symptoms	1
Jejunostomies for Duodenal or Pyloric Ulcer	3
Deaths	1, or 33⅓%
Recovered	2
Relief of G I symptoms	2
Resection for Massive Hemorrhage	6
Deaths	6

operations The cause of death was pneumonia in 13, hemorrhage in 8, wound disruption in 7, peritonitis in 5, shock in 5, and the rest died of other causes

With the exception of the marginal ulcer group, the mortality was high Another outstanding fact was that of the patients who recovered from the gastric resection only three had recurrences whereas gastro-enterostomy alone gave freedom from symptoms in less than 65 per cent of the cases

DR RICHARD LEWISOHN (New York) was in complete accord with Doctor Cutler but not quite so fully with Doctor Eggers Among the points mentioned by Doctor Eggers was that gastro-enterostomy is a side-tracking operation and that it reduces the acidity in the stomach, which Doctor Lewisohn assumed to mean that high acidity is reduced to a very low minimum In Doctor Lewisohn's experience gastro-enterostomy does not side-track the food and does not reduce the acidity Doctor Eggers reported his mortality for gastro-enterostomy somewhere between 4 and 5 per cent Doctor Lewisohn's mortality for gastric resection in primary gastroduodenal ulcers has always been below 4 per cent, but he admitted selecting his cases just as carefully as Doctor Eggers and Doctor Cutler have done

Doctor Lewisohn was a little surprised at the lack of careful and detailed follow-up data on Doctor Eggers's patients Many years ago, at the Mt Sinai Hospital, gastro-enterostomy was regarded as a satisfactory procedure, until there was instituted a very careful follow-up study including roentgenologic studies

Doctor Lewisohn felt that every experienced surgeon was performing gastro-enterostomies in about the same way In proof of this, the facts are that in many parts of the world, including Sweden, Italy and elsewhere, surgeons are obtaining a high percentage of gastroduodenal ulcers after gastro-enterostomy, and he wondered if "conservative" is the right word for the procedure of gastro-enterostomy, and whether it is not really more conservative, in view of the postgastro-enterostomy complications (hemorrhage and recurrent ulcer) to perform a primary, partial gastric resection, which is really the more conservative operation because, in a majority of cases, the cure is definite and permanent

DR FREDERIC W BANCROFT (New York) said that with passing years there had been a great deal of progress with regard to surgery for peptic ulcer, and that the papers presented brought out the real fact or reason for the changing attitude toward this branch of surgery Fifteen years ago surgery was not being performed upon medical failures in peptic ulcer but for any type of duodenal ulcer that came into a surgical ward Today the type that comes to surgeons in clinics like that of the Roosevelt or Lenox Hill Hospitals is a medical failure—the patients who have been given adequate medical care over a long period of time without permanent relief In considering medical treatment it is necessary that a patient should have had an adequate period of rest in bed With the edema and swelling of the gastrohepatic membrane secondary to lesser curvature ulcer, rest is necessary in order to relieve the tension resultant from the full stomach on an inflamed membrane It is necessary to place the area of inflammation at about the level of the heart so that venous out-flow is facilitated and edema diminished If surgery is required, then, for an ulcer that has resisted medical treatment, the surgical procedure is of necessity more radical The indications for surgery are either repeated hemorrhages, marked indurated ulcerations without retention, which resist medical therapy, or scar tissue

contraction with obstruction. In the first two, probably resection is advisable, while in the last gastro-enterostomy is usually the operation of choice.

DR JOHN A. MCCREERY (New York) thought that the difference of opinion as to the proper procedure in these cases seemed to him to be due largely to the fact that the ideas as to the etiology of peptic ulcer were still vague, and that surgery was a matter of operating upon symptoms which may recur, as the underlying cause was still present. However, the work that is being done seems to be along generally similar lines and gradually, though more or less deviously, the same conclusions were being approached.

Doctor McCreery said that the experience and the trend of thought at Bellevue Hospital followed very closely those outlined by Doctor Cutler. It is believed at Bellevue that no case should be considered surgical in the absence of an acute complication, such as perforation, until prolonged medical treatment has failed. In this connection it is interesting to note that it is the experience of the Gastric Clinic, which is presided over by surgeons, that only about five per cent of their cases ultimately come to operation. These figures cover individuals in the lowest income group, with the least opportunity for proper rest and diet, and should be bettered in the higher income group. It is in the group of cases, with uncomplicated duodenal ulcer, carried along fairly comfortably in the clinic, that gastro-enterostomy, in the past, was more frequently performed than at the present time. It was successful for two reasons. In the first place, it supplied a safety valve in the case of subsequent pylorospasm, and in the second place, the patient who had undergone an operation for ulcer was more apt to be impressed by the seriousness of his disease and the importance of care in diet than the patient who has been carried through repeated attacks on a medical regimen. If one omits this group of cases and considers as operable only those with complications—hemorrhage, obstruction, intractability—it seemed to Doctor McCreery that the percentage of cases in whom relief can be expected from gastro-enterostomy must be distinctly lowered. It was his feeling that in this group, only those with obstruction and low acidity are primarily candidates for gastro-enterostomy. Hemorrhage and intractable pain, especially if due to chronic perforation seemed to Doctor McCreery to demand a more radical procedure. "Follow-up" in this group of cases is most important and the final results are difficult of estimation. He had recently reported cases of perforation well for ten years who had returned with symptoms of ulcer. In the last month he had seen two cases in whom gastro-enterostomies for duodenal ulcer had been performed in 1924. They had been followed regularly in the clinic for seven years and then closed. Both had developed gastric symptoms during the past few months, 14 years after their original operation. One has a contracted stoma, with retention. The other is still being studied. Cases such as these make it difficult to say when a case is "cured", and rather force one to agree with Means, when he said last fall, in Chicago, "Moreover if the surgeon is called in and operates, the physician will still have to care for the patient for the rest of his life, because surgery usually does not cure the patient with ulcer any more than does medicine."

DR DEWITT STETTEN (New York) said that the subject of peptic ulcer was always a live one. To-day agreement is more or less general that peptic ulcer is primarily a medical disease and that every effort should be made to heal the ulcer by medical measures before surgery is resorted to. Agreement is also general that in spite of the most conscientious medical treatment certain cases eventually become surgical. The surgical indications were very

clearly presented by Doctor Cutler. He congratulated Doctor Eggers for having the courage to take up the cudgels in defense of the somewhat discredited operation of gastro-enterostomy, and was inclined to agree, in some respects, with his thesis. Gastrectomy, not necessarily always subtotal, he felt to be definitely indicated for obvious reasons in all surgical cases of chronic gastric or pyloric ulcer when technically feasible. It may also be indicated in an occasional favorable case of early perforation, when the patient's condition warrants the procedure. It is also indicated in chronic infiltrated ulcers of the duodenum, penetrating into the pancreas or toward the liver, and for cases in which there has been profuse hemorrhage from involvement of large blood vessels, provided the technical difficulties of the operation are not too great and the patient's life is not placed in jeopardy by the procedure.

Sometimes a two-stage procedure may be advisable—primary gastro-enterostomy, followed by partial or subtotal gastrectomy, after the patient's condition has improved and some of the inflammatory reaction around the ulcer has subsided. Gastrectomy is usually indicated in secondary marginal ulceration after gastro-enterostomy. For healed ulcers at the pylorus or in the first portion of the duodenum, with cicatricial stenosis, Doctor Stetten believed that posterior, short-loop retrocolic gastro-enterostomy—in preference to pyloroplasty—is the operation of choice, and probably gives the most satisfactory results obtainable in gastric surgery. In this connection he cited a statement that he made in a discussion at a "Symposium on Gastric and Duodenal Ulcer," held before the Clinical Society of Lenox Hill Hospital, in the fall of 1926. "I know of no other operation upon the stomach, not excluding subtotal gastrectomy, in which the immediate postoperative recovery is usually so easy, in which the end-results are so uniformly satisfactory and gratifying, and in which the patient is so permanently and thoroughly cured as by this operation performed for this disease." Doctor Stetten's experience during the past 12 years had not altered his opinion, but rather confirmed it.

Subsequent ulceration in the stomach, pylorus or duodenum, in the jejunum or at the gastro-enterostomy stoma, after gastro-enterostomy for cicatricial stenosis, is in our experience extremely rare, possibly because in these cases the ulcer diathesis has ceased to exist. He also still favored gastro-enterostomy in those cases of duodenal ulcer where resection would be too difficult or too dangerous, especially because of their too close proximity to the papilla of Vater, and in perforated pyloric and duodenal ulcers where a stenosis is produced by the suture closing the perforation, providing the perforation is not older than 12 hours and the patient's condition is favorable. Although he had not yet made a thorough statistical study of his material, his experience with gastro-enterostomy in properly selected cases of this group, with proper after-cure, had not been unsatisfactory. He admitted having had an occasional recurrence of symptoms, especially of bleeding, and had seen a number of jejunal and marginal ulcerations, but, off-hand, the percentage of jejunal and gastrojejunal ulcers certainly had not exceeded 4.5 per cent, which is the incidence of this complication, established by Lahey and Jordan in a statistical study of nearly 17,000 gastro-enterostomies, performed by different surgeons in various countries, and which is a little more than the statistics of Eusterman and Balfour, namely 3 to 4 per cent. Doctor Stetten said he certainly had seen nothing remotely approaching the 34 per cent frequency that has been reported from the Mt Sinai Hospital. Incidentally, since subtotal gastrectomy for ulcer has in recent years become so much more popular, and the opportunity has been presented for more extensive follow-up

studies, gastrojejunal and jejunal ulceration also, after this operation, has been found to be much more frequent than was originally supposed to be the case. Sawkoff in a recent compilation from the Russian literature found the incidence to be 4.32 per cent, practically the same as that recorded by Lahey and Jordan, and even more than that noted by Eusterman and Balfour after gastro-enterostomy. It is questionable whether gastro-enterostomy is of any value in unresectable, lesser curvature ulcers.

DR CARL EGGERS (closing) referred to Doctor Lewisohn's comment, particularly on the lack of detailed follow-up, and explained that this had been omitted simply because it would have made too long a table. The cases are spread out over many years. Those reported in the paper represented Doctor Eggers' personal experience with gastro-enterostomy. He has followed all of his patients, except a few in the early age-group to which he called attention, and who had drifted away, for a very long time. Some of these early cases were of the high strung nervous temperament, that those who deal with this type of condition are familiar with. They were well when discharged and for a long time after, though a few may not have remained well. The results of the later cases are stated in the paper which Doctor Eggers did not read in full detail.

With regard to side-tracking, Doctor Eggers emphasized that gastro-enterostomy was conceived as a side-tracking operation. It was devised for obstruction of the pylorus and was used at first for carcinoma and later for ulcer. In Doctor Eggers' opinion, gastro-enterostomy to-day gives the very best results in the patients in whom it brings about a side-tracking and shunts out the pylorus because of obstruction. The case with the fistula of the biliary tract which he presented, shows that beautifully, all the food empties through the gastro-enterostomy, one can watch it pass through the stoma.

Doctor Eggers could not concur that primary resection was a conservative operation for duodenal ulcer. Although Doctor Lewisohn has fine results and is to be congratulated, nevertheless when one is teaching this subject one is on dangerous ground to teach that half the stomach—and that is usually not conceded to be enough—should be resected. The mortality will be high in the hands of men who only occasionally see a case of peptic ulcer requiring surgery. Even though a jejunal ulcer does develop in 3 or 4 per cent of the cases, they can be handled by the original surgeon or turned over to another more experienced one. Furthermore, such a patient may at that time be an entirely different type of patient, years after the original gastro-enterostomy, and, therefore, one to be handled in an entirely different way.

Doctor Eggers said most of his patients are of the older age-group, they are not young patients, but people who have had adequate medical treatment, and in these gastro-enterostomy has been a most successful method of treatment. He lost two patients in whom he performed a resection because roentgenographically there was a suspicion of carcinoma and he felt he might have saved them had he performed a gastro-enterostomy only. Gastro-enterostomy usually relieves the patient even if no anacidity is produced. After all, the aim in medicine is not to produce anacidity but to relieve symptoms or to cure the patient. Doctor Eggers stated that he had no objection to resection of the stomach and that he likes the operation very much, but does not believe that routine resection of the stomach is the ideal operation for a duodenal ulcer. Surgeons should cultivate judgment and apply it in each case in order to insure the best results.

POSTOPERATIVE JEJUNAL ULCER

A STUDY OF TWENTY-THREE CASES OPERATED UPON AT THE PRESBYTERIAN
HOSPITAL, NEW YORK

ABRAHAM GROSSMAN, M D

CHICAGO, ILL

WITH the extensive development of gastric surgery in the past 50 years a new clinical entity has become recognized, namely, postoperative jejunal ulcer. Primary jejunal ulcer, a solitary lesion of the upper jejunum, not preceded by gastrojejunostomy and occurring in the absence of such diseases as typhoid, amebic or bacillary dysentery, cholera, tuberculosis, syphilis and sepsis, is exceedingly rare. Judd¹ has never seen a case and questions its existence. Ebeling,² in a thorough review of the subject, concluded that primary jejunal ulcer is a most infrequent lesion. Not so, however, relative to the occurrence of jejunal ulcer following gastric surgery.

The first authentic case of postoperative jejunal ulcer was reported by Braun,³ in 1889. From that time on, the condition has been diagnosed with increasing frequency, depending upon the interval after operation and the thoroughness with which surgeons have followed their patients subjected to gastro-intestinal surgery. Paterson,⁴ in 1909, found but 52 undisputable and ten doubtful cases of jejunal ulcer reported in the literature. Eustermann,⁵ in 1920, found 83 cases following various gastric operations performed at the Mayo Clinic. This did not include many cases in which the lesion had healed without requiring surgery. Until recently, it has been felt that jejunal ulcer could be avoided by performing an extensive resection instead of a gastro-enterostomy. Two schools have arisen defending the one operation and condemning the other. The advocates of gastrectomy (von Haberer,⁶ Finsterer,⁶ Berg,⁷ Strauss⁸ and others) have estimated the incidence of jejunal ulcer following gastro-enterostomy as varying from eight to 30 per cent. These authors claim a much lower percentage following resection (1 per cent or less). With the increase in popularity of the more radical operation, it has proved to be more productive of jejunal ulcer than was formerly suspected. Balfour,⁹ in 1928, reported 28 cases upon which he had operated for jejunal ulcer following gastrectomy. Cames¹⁰ has reported four cases of jejunal ulcer following a procedure resembling the Polya operation, which is considered a nearly ideal form of gastrectomy. Hurst¹¹ has collected over 100 cases of secondary ulcer following gastrectomy. Advocates of resection maintain that in such cases the resection may have been inadequate. However, the development of jejunal ulcer has been reported even after subtotal resection (Holst¹²).

It is evident that factors other than the operative procedure employed

may have some influence on the development of jejunal ulcer. Such factors fall into three groups (1) Preoperative, (2) operative, and (3) postoperative.

Preoperative Factors—Of these the outstanding is *the indication for operation*. The more definite the indications for operation in peptic ulcer, the less the likelihood of postoperative jejunal ulcer. Such indications have not yet been infallibly defined (excluding from consideration acutely perforated ulcers). However, the consensus of opinion is that the best results occur in cases that have had a lengthy course of vigorous medical treatment, with symptoms responding less and less to such treatment, and characteristic of the late complications of peptic ulcer, such as obstruction, penetration or uncontrollable bleeding (Moynihan¹³).

Another factor of importance is *the location of the original ulcer*. Since

duodenal ulcer as opposed to gastric is more regularly accompanied by hyperacidity (Lindau and Wulff,¹⁴ Huist and Stewart¹⁵), it is to be expected that cases of duodenal ulcer coming to operation may be followed by a higher incidence of jejunal ulcer than cases of gastric ulcer. The vulnerability of the jejunal mucosa to highly acid gastric juice has long been recognized (McMaster¹⁶).

Operative Factors—Under this category a number of points must be considered. The most important of these is the degree of neutralization of gastric acidity accomplished by the operative procedure. Moynihan,¹³ and Judd¹ maintain that persistent hyperacidity following operation is the most important single cause of postopera-

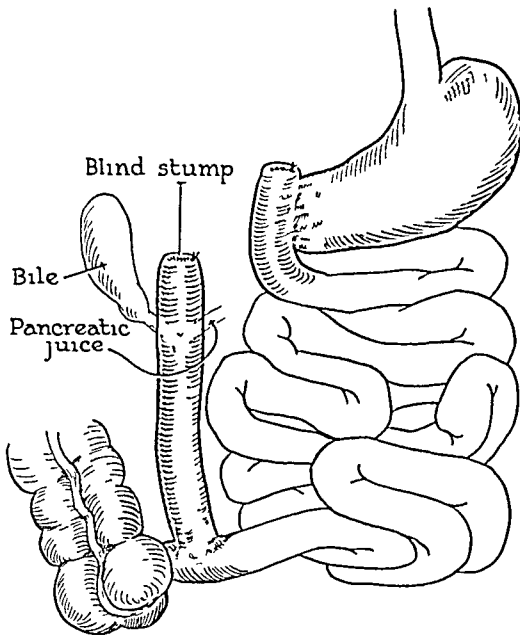


Fig 1.—Diagrammatic sketch showing how the Mann-Williamson operation deviates the bile, pancreatic juice and duodenal secretion into lower ileum leaving the jejunum exposed to unneutralized gastric juice.

tive jejunal ulcer. The only reliable way of producing chronic peptic ulcer in animals is to deviate alkaline juices from the site of gastrojejunostomy. This has been done repeatedly by the Exalto¹⁷ procedure, which in this country has become known as the Mann-Williamson¹⁸ operation (Fig 1).

Such an operation as illustrated in Fig 1 deviates the bile, pancreatic juice and duodenal secretions from the site of gastrojejunostomy, exposing the jejunum to the action of unneutralized gastric juice. Mann and Williamson¹⁸ found this procedure produced jejunal ulcers in 95 per cent of their dogs. Their results have been confirmed by Ivy and Fauley,¹⁹ Matthews and Dragstedt,²⁰ Gallagher and Palmer,²¹ and many others.

Entero-enterostomy when combined with gastro-enterostomy and the Roux en Y type of anastomosis produces a similar deviation of alkaline juices (Figs 2 and 3).

Finsterer¹⁷ reported the development of jejunal ulcer in seven out of eight patients upon whom he performed the Roux en Y operation. When the anastomosis was taken down and the original anatomic relations restored, the jejunal ulcer healed in all the cases. Paterson²² was one of the first to indicate the dangers of Y-anastomosis and entero-enterostomy.

Another factor of importance is the physiologic principle, worked out by Matthews and Dragstedt,²⁰ that the lower the loop of small intestine the greater its vulnerability on exposure to gastric juice. Accordingly, anterior gastro-enterostomy may be expected to result in a higher incidence of jejunal ulcer than posterior gastro-enterostomy because a lower loop of jejunum comes into contact with gastric juice.

The importance of unabsorbable suture material as a factor in the development of jejunal ulcer is discussed at the end of Case 2.

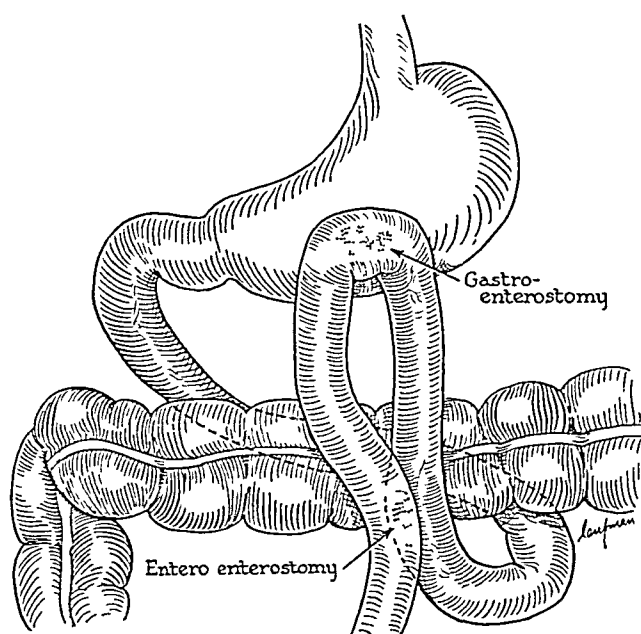


FIG 2—Diagrammatic sketch showing how entero-enterostomy when combined with gastro-enterostomy deviates the protective alkaline juices leaving the jejunum at the site of gastrojejunostomy exposed to unneutralized gastric juice.

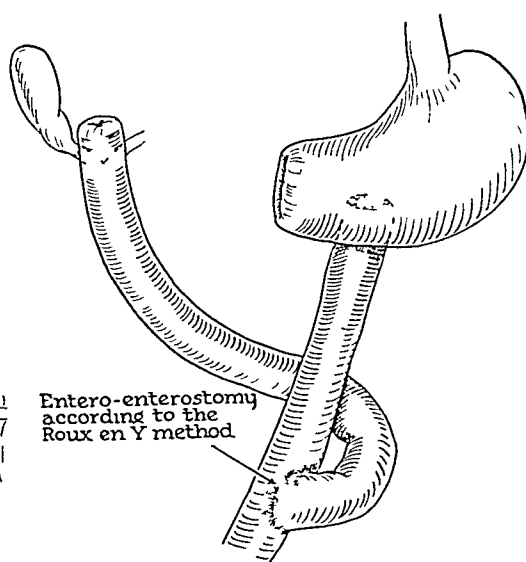


FIG 3—Diagrammatic sketch showing how the Y type of anastomosis produces the same physiologic conditions as the Mann-Williamson operation.

The use of clamps, hematoma of the suture line and traumatic erosions of mucosa at the time of operation cannot be considered significant factors in the development of jejunal ulcer because of the rapidity with which such traumatic lesions heal and the length of time before chronic jejunal ulcers develop (Ivy and Fauley,¹⁹ and Gallagher and Palmer²¹).

Moynihan,¹³ and Burden²⁷ have emphasized the importance of removing the appendix at the time of operation for peptic ulcer. The association of appendiceal disease and pylorospasm and the rôle of pylorospasm in preventing regurgitation of alkaline juices needed for neutralization of gastric acidity has been seriously considered a potential factor in the development of peptic ulcer (Elman²⁶). However, the importance of appendectomy at the time of surgery for peptic ulcer is still a matter of conjecture.

Postoperative Factors—Following surgery for peptic ulcer numerous fac-

tois come into play which may contribute to the later development of jejunal ulcer. These are mainly matters of diet, habits and latent foci of infection.

Diet—The natural expectation of a patient just operated upon for peptic ulcer is that the disease is cured and there will be no further need of adhering to a diet. This is far from the true state of affairs. Dietary irregularities are among the most frequent precipitating causes of recurrent symptoms following gastric surgery and may play an important rôle in the later development of jejunal ulcer.

Alcohol—Alcohol is such an excellent stimulus for the flow of gastric juice that it is occasionally used for estimating gastric function (Ehrmann test meal). For further information concerning the detailed action of alcohol on the gastric mucosa the reader is referred to summaries by Leddig,²⁸ Himmwich,²⁹ Kast³⁰ and Chittenden.³¹ Excessive intake of alcohol may influence the formation of postoperative jejunal ulcer.

Tobacco—Moynihan³³ has demonstrated the increased output and increased acidity of gastric juice after smoking. It is a common statement of ulcer patients that smoking aggravates their symptoms. Circulatory insufficiency in the pyloric area has been considered of some importance in the etiology of peptic ulcer (Reeves,³² Payl,³³ and Gallagher³⁴). The relation of tobacco to vasospastic phenomena (tobacco angina, intermittent claudication in Buerger's disease) has long been recognized. Its relation to jejunal ulcer naturally becomes a matter of interest.

Latent Foci of Infection—Konjetzny,³⁵ Turck,³⁶ Rosenow,³⁷ Meisser,³⁸ and others have investigated the possibility that bacteria (particularly the *Streptococcus* and possibly the *Bacillus coli communis*) may be related to the development and persistence of peptic ulcer. Latent foci of infection may be considered as contributory factors in the pathogenesis of postoperative jejunal ulcer.

With the above general principles in mind, 23 cases of postoperative jejunal ulcer operated upon at the Presbyterian Hospital, New York, were studied in minute detail from the time of appearance of the original duodenal or gastric ulcer symptoms, through operation, to the ultimate status of the patients at the present time. In several additional cases the diagnosis of jejunal ulcer had been made at one time or another, but the evidence was not sufficiently conclusive to merit their inclusion in this study. Twenty-three cases is a small number. However, it is hoped that similar studies of postoperative jejunal ulcer may become more frequent, in the hope of gaining a better understanding of this complication of gastric surgery and a method of minimizing its occurrence. Of these 23 cases nine had their primary operations for peptic ulcer at some other hospital.

A number of them illustrate well the physiologic principles involved in the pathogenesis of jejunal ulcer and are, therefore, presented in some detail.

Case 1—No. 80855. I. H. first experienced severe digestive symptoms at the age of 22. These consisted of gnawing pain in the epigastrium, coming three to four hours after meals, and relieved by food or alkaline powders. Four years after the onset of

these symptoms he was admitted to the Presbyterian Hospital. The gastric contents were somewhat hyperacid (free, 40, total, 80). The Lenhartz diet afforded relief from symptoms. The patient refused to remain on diet, consequently he was operated upon January 21, 1912. The anterior duodenal wall just distal to the pylorus showed a scar. The duodenum was plicated between the pylorus and the site of the ulcer and posterior gastro-enterostomy was performed. He then was well for six years, at which time digestive symptoms recurred. These resembled the preoperative symptoms except that the pain and abdominal tenderness were now situated to the left of the umbilicus. These symptoms responded to diet and the patient remained fairly comfortable until a severe recurrence of abdominal pain 17 years postoperatively. Roentgenograms taken at periodic intervals during these 17 years had been negative. Films taken at this time, however, showed a jejunal ulcer. At operation, August 16, 1929, a gastrojejunocolic fistula was found. The anastomosis was taken down, and the stomach, jejunum and transverse colon were repaired. On the eleventh day the wound disrupted and secondary closure was necessary. The following day intestinal obstruction developed and ileostomy was performed. The patient died the following day.

Comment—This patient did well for six years after operation. It is possible that the duodenal plication by closing the pylorus created a greater need for the new stoma. It has been claimed that those patients do better after gastro-enterostomy in whom the pylorus is least patent. Not until 17 years postoperatively was there roentgenologic evidence of jejunal ulcer. This illustrates the fallacy of figures based on five- or even ten-year observation following gastric surgery.

Case 2—No 85764. W. P. first developed ulcer symptoms at the age of 29. Four years later he was operated upon elsewhere. A duodenal ulcer was found. Posterior gastro-enterostomy and appendectomy were performed. Within three months his symptoms recurred, and two years later he presented himself at the Presbyterian Hospital because the pain had become unbearable. He was reoperated upon 28 months following the gastro-enterostomy. A linen suture was discovered running through a sinus between gastric and jejunal walls above the stoma with an ulceration at the jejunal orifice of the sinus. The operation consisted in dissolution of the gastro-enterostomy and restoration of the original anatomic and physiologic relationships.

Comment—In this case, operated elsewhere, jejunal ulcer may have been due to the use of unabsorbable suture material. Moynihan¹³ believes that unabsorbed suture material may be a cause of jejunal ulcer. Eustermann⁵ found that in one-third of the jejunal ulcer cases on record at the Mayo Clinic unabsorbable suture material had been employed. Woolsey²⁴ has reported a case similar to this one in which unabsorbed suture material was found hanging from the stoma 21 months after gastro-enterostomy.

Case 3—No 242133. T. D., age 41, was admitted to the Presbyterian Hospital because of repeated attacks of vomiting. He was a moderately severe, insulin-treated diabetic, who had been in the hospital several times previously because of acidosis, each attack being accompanied by vomiting. His vomiting at the time of his present admission presented a diagnostic problem. Roentgenologic examination showed 25 per cent six hour retention and suggested obstruction just beyond the pylorus. He was operated upon September 10, 1930, an indurated scar was seen on the anterior surface of the duodenum. The pylorus was patent. A posterior gastro-enterostomy was performed. A roentgenogram taken postoperatively showed the new stoma to be functioning well, no

barium passed through the pylorus. He was well for two years at which time he returned because of uncontrollable vomiting. Fluoroscopy revealed constriction of the efferent jejunal loop and a vicious circle, i.e., reflux of barium into the stomach via the pylorus. Gastric lavage provided only slight relief and he was again operated upon October 14, 1932, two years after his primary gastro-enterostomy. A jejunal ulcer was found 25 by 15 cm, adherent to the transverse colon and mesocolon. The gastro-enterostomy was taken down, gastric and jejunal openings and mesocolon repaired, and side-to-side jejunojejunostomy performed between the two loops of jejunum on either side of the ulcer-bearing segment. The postoperative course was uneventful. Two months later he returned because of postprandial pain and vomiting. Roentgenologic examination showed reactivation of the old duodenal ulcer and a 20 per cent gastric retention. The symptoms responded to a modified Sippy diet, gastric lavage with removal of the residue at night and belladonna. On this regimen the patient has remained well for over two years after reactivation of the same duodenal ulcer for which he was originally operated upon.

Comment—This case is unusual because of the rarity with which duodenal ulcer and diabetes coexist.⁴⁰ The dietary situation in such cases is extremely difficult to handle. Often, as in this case, when vomiting occurs while the diabetes is not fully controlled, a diagnostic problem arises. In spite of an ideal indication for surgery initially (cicatrical obstruction), jejunal ulcer developed in less than two years. What proportion of the obstruction may have been due to spasm one cannot say, for belladonna was not tried therapeutically. The duodenal ulcer newly reactivated after dissolution of the gastro-enterostomy, and again with symptoms of obstruction, remains under control with lavage and belladonna. The case suggests that if the indication for operation be obstruction, it is essential to determine by the use of antispasmodics whether cicatrical obstruction or only spasm exists.

Case 4—No 47876. M. G. first developed peptic ulcer symptoms at the age of 34. She was treated medically for three months with partial relief. There was no obstruction or evidence of bleeding. Atropine was not tried. She was operated upon October 29, 1920. Duodenal ulcer was visualized. Partial gastrectomy combined with a Y-anastomosis was performed, the appendix was removed. She remained well for three years following operation despite lack of adherence to diet. At this time she returned with a recurrence of her original symptoms. Roentgenologic studies revealed a crater in the jejunal loop, below the stoma, with marked overlying tenderness. After three weeks of Sippy regimen her pain disappeared. Fluoroscopy showed the crater persisting but no tenderness. She is still in excellent health, 13 years after her operation. She has been systematically followed by letter and reports occasional, slight digestive discomfort, which has always responded to the administration of an alkali.

Comment—Despite a Y-anastomosis, this patient is practically free of digestive symptoms, 13 years after operation. The fact that a partial gastrectomy was performed along with the anastomosis may have had some bearing on its success. It is interesting that the one examination of her fasting gastric contents, postoperatively revealed an anacidity, whereas, usually this type of gastro-enterostomy, without resection, results in hyperacidity.

Case 5—No 69908. A. K., age 29, was admitted to the Presbyterian Hospital because of pain of two weeks' duration beginning in the umbilical region and radiating to the right midback. He had been jaundiced five years previously. Gallbladder disease

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was suspected. He was operated upon August 7, 1909. The gallbladder was normal. The anterior wall of the stomach, on the lesser curvature, well up near the cardia presented an indurated, puckered scar. Anterior gastro-enterostomy was performed because of a short gastrocolic omentum. The postoperative course was uneventful. The patient remained well for 18 years at which time he was readmitted, seriously ill, presumably due to a perforated jejunal ulcer and was operated upon immediately. A perforated jejunal ulcer was found on the anterior margin of the stoma adherent to the liver. The stoma and ulcer-bearing segment of jejunum were excised and the opening in the stomach repaired. The stomach was then brought through the mesocolon and sutured to the distal loop of the transected jejunum by side- (of stomach) to-end (open end of jejunum) anastomosis. The proximal loop of transected jejunum was anastomosed to the distal jejunal limb about 6 cm below the gastrojejunostomy. This left essentially a Roux en Y anastomosis without pyloric occlusion. The postoperative course was uneventful. He has adhered to a proper diet and has in general remained well for seven years.

Comment—Despite anterior gastro-enterostomy, an operation predisposing to subsequent marginal ulcer, this patient went 18 years without digestive symptoms before returning with a perforated jejunal ulcer. This again shows the futility of five- and ten-year follow-up statistics on ulcer cases. Though left with a physiologic arrangement (Roux en Y), which deviates alkaline juices below the stoma, this patient has gone seven years without evidence of a marginal ulcer. The fact that his original ulcer was gastric in location, and quite some distance from the pylorus may bear some relation to his failure to develop jejunal ulcer following a Roux en Y anastomosis.

Case 6—No 71401. L. T. first developed peptic ulcer symptoms at the age of 20. He was treated dietetically for five years during which time there were frequent remissions and exacerbations of symptoms. Upon his third admission to the Presbyterian Hospital (over five years after onset of ulcer symptoms) roentgenologic examination showed a 60 per cent residue after six hours. Atropine was not tried. At operation the duodenum was so bound down by adhesions that it could not be seen. The gastrocolic omentum was short, anterior gastro-enterostomy was performed, followed by entero-enterostomy to prevent stasis in the long afferent limb. Within a month he returned because of severe pain beginning to the right of the umbilicus and radiating to the right sub-costal margin. Roentgenologic examination revealed a jejunal ulcer 2 cm below the stoma in the distal jejunal loop. Histamine test showed free acid, 98, total acid, 120. After three weeks of bed-rest and Sippy diet supplemented by moderate doses of atropine, the symptoms disappeared, and control roentgenograms no longer showed evidence of jejunal ulcer. The patient left the hospital only to return for his fifth admission, 16 months later, because of a severe relapse. Roentgenologic examination again revealed the jejunal ulcer previously visualized. It seemed best to remove the ulcer-bearing segment of jejunum in order to prevent acute perforation at a later date. At operation, a jejunal ulcer was found, which had produced adhesions between the ulcerated portion of jejunum and parietal peritoneum. The portion of efferent jejunal limb bearing the ulcer was excised and the cut ends of the gut were inverted. The gastro-enterostomy and entero-enterostomy stomata were patent and were left undisturbed. Convalescence was uneventful. There has been no recurrence of symptoms to date (19 months postoperatively).

Comment—The outstanding feature of this case is the rapidity with which jejunal ulcer occurred when gastro-enterostomy was combined with entero-enterostomy. It illustrates the greater vulnerability of low loops of

jejunum Entero-enterostomy undoubtedly contributed to the formation of a jejunal ulcer by deviating alkaline juices from a segment of jejunum needing them most In this case intensive medical therapy not only relieved the symptoms of the jejunal ulcer but caused the disappearance of the roentgenologic findings in three weeks

Case 7—No 333264 J W first experienced symptoms characteristic of peptic ulcer at the age of 16 These continued intermittently for 13 years before he was hospitalized At the time of his admission to the Presbyterian Hospital in March, 1932, roentgenologic examination showed a deformed duodenal bulb and a 25 per cent gastric retention after six hours The gastric contents showed free acid, 84, and total, 98, after histamine stimulation Rest in bed and a Sippy regimen did not relieve the pain At operation, March 22, 1932, a dense scar was seen on the anterior duodenal wall, posterior gastro-enterostomy with entero-enterostomy was performed He was discharged, relieved, on the seventeenth day after operation Ten months later the abdominal pain and nausea returned Roentgenologic examination at this time showed a jejunal crater halfway between gastro-enterostomy and entero-enterostomy stomata He was placed on an ambulatory ulcer diet Three weeks later he was admitted with an acute surgical abdomen and was operated upon immediately There had been a fresh perforation of a jejunal ulcer into the transverse mesocolon The perforation was sutured and the abdomen closed Convalescence was uneventful To date the patient has remained well

Comment—This was an ideal case for surgery, the history was of long standing (13 years), the response to medical treatment was becoming less and less, there was evidence of pyloric obstruction, the gastric contents were hyperacid However, when entero-enterostomy was combined with gastro-enterostomy jejunal ulcer developed within a year

Case 8—No 397854 A A developed symptoms of bleeding peptic ulcer at the age of 24 Roentgenologic studies done elsewhere revealed a duodenal ulcer He was placed on a Sippy regimen for two months during which time the symptoms were only moderately alleviated Posterior gastro-enterostomy was then performed elsewhere, in 1927 He remained well for two years at which time his symptoms recurred He was hospitalized and placed on a Sippy regimen for ten days, and was completely relieved, remaining so for two years He was again hospitalized elsewhere because of a severe relapse Roentgenograms indicated pyloric occlusion He was reoperated upon, and the pyloric occlusion verified A Billroth II resection was performed He was then well for two years at which time symptoms recurred, and were worse than any he had experienced before He was admitted to the Presbyterian Hospital Roentgenologic examination revealed a marginal ulcer producing moderate obstruction Medical therapy afforded no relief and the patient was operated upon December 6, 1933 Two centimeters from the distal end of the gastro-enterostomy stoma was an indurated jejunal ulcer which was densely adherent to the transverse mesocolon The stoma was widely patent and was left *in situ*, the operation consisting of resection of the ulcer, repair of the jejunum and side-to-side entero-enterostomy between the afferent and efferent jejunal limbs This left essentially a Y-type of anastomosis The postoperative course was uneventful Three weeks later the patient returned because of severe postprandial pain Roentgenograms taken at this time, and repeated a month later, showed a constricted jejunum, a jejunal crater with overlying tenderness, indicative of jejunal ulcer The pain disappeared after rest in bed, Sippy regimen, atropine and luminal The patient has not been heard from since

Comment—Despite gastrectomy (Billioth II), jejunal ulcer developed within two years. Secondary operation for obstruction from this jejunal ulcer included entero-enterostomy in a jejunum which had already shown itself predisposed to ulcer formation. This deviation of alkaline juices must have played an important rôle in the unusually rapid development of the second jejunal ulcer, three weeks after entero-enterostomy.

Case 9—No 59085 B R first developed ulcer symptoms at the age of 22. The symptoms could be controlled by dieting and alkali, and it was not until two years later that he was first seen in the Presbyterian Hospital because of an acute attack of epigastric pain and vomiting. Roentgenologic examination revealed a deformed duodenal bulb and 15 per cent retention at the end of six hours. He remained in the hospital for two months and was discharged on an ambulatory ulcer diet. As long as he adhered to it he was well. Unfortunately, his lack of will power led to frequent departures from the diet, each followed by a recurrence of symptoms. He was operated upon April 3, 1925, following a particularly severe episode of pain. A small scar was noted on the lateral wall of the first portion of the duodenum. A posterior gastro-enterostomy with entero-enterostomy was performed. He did not adhere to diet after discharge and six months later returned because of severe postprandial pain. Roentgenologic examination at this time showed a crater in the efferent jejunal limb, 1 cm below the stoma. During the five years subsequent to the development of this marginal ulcer the patient has been in and out of this hospital and numerous others, leading a miserable life, except during spasmodic periods of adherence to a strict diet, alkali and belladonna.

Comment—Since gastro-enterostomy entails at least a temporary period of dieting postoperatively, such surgery is hazardous upon an individual who has shown himself unwilling to adhere to medical measures unless extreme indications for operation exist.

Case 10—No 250685 M B underwent an appendicectomy elsewhere, at the age of 25. The abdominal pain for which he was operated upon persisted, and three months later he was reoperated upon in Dublin for "pyloric obstruction." Posterior gastro-enterostomy was performed. He remained well for two years, during which time he came to this country. He attended the G I Clinic of the Presbyterian Hospital from 1926 to 1929, during which time he had many attacks of severe pain in the hypogastrium and left iliac regions, several tarry stools and occasional hematemesis. These symptoms usually responded to dietary measures. Several roentgenologic examinations were made during this three-year interval but failed to show a marginal ulcer until December, 1929, at which time the gastro-enterostomy stoma had closed off completely. He was operated upon January 6, 1930, at which time a scarred jejunum, adherent to transverse colon and mesocolon was found. The operation consisted of taking down the anastomosis, closing the opening in the stomach, resecting the stoma and ulcer-bearing segment of jejunum and reestablishing jejunal continuity by end-to-end anastomosis. One month after discharge from the hospital digestive symptoms recurred. Roentgenologic examination one year after operation showed a reactivation of an old duodenal ulcer. Diet, alkali and belladonna usually afforded relief, but the patient would not adhere long to any regimen. He was, therefore, readmitted for operation June 12, 1934, four and one-half years after operation for the jejunal ulcer. The duodenum was so imbedded in adhesions it could neither be seen nor felt. The transverse mesocolon was short and adherent. It seemed best to section the stomach in the pars media, turn in the distal loop, physiologically excluding the duodenum, and then perform an end-to-side, long-loop, anterior gastro-enterostomy and entero-enterostomy. He convalesced rapidly and left the hospital on the eighteenth day. Two weeks later he returned to the hospital because of low thoracic

pain, thought to be pleuritic in origin. Strapping gave no relief. Roentgenologic examination showed no pleural or pulmonary pathology, but that of the GI tract showed a persistent crater just below the gastro-enterostomy stoma in the efferent jejunal limb. With liberal doses of alkali and atropine the symptoms disappeared as did the crater seen roentgenologically. At the present time, the patient has just been readmitted because of a recurrence of severe pain. The jejunal ulcer is again visible roentgenologically.

Comment—The rapidity with which jejunal ulcer developed in this case illustrates the danger of deviating the gastric contents to a low segment of jejunum, particularly when this segment is deprived of protective alkaline juices by entero-enterostomy. There is an opportunity to compare the length of time it took this patient to develop jejunal ulcer after two different types of gastro-enterostomy. Originally, with a posterior gastro-enterostomy, he went for six years before developing roentgenologic evidence of jejunal ulcer, whereas, after anterior, long-loop gastro-enterostomy combined with an entero-enterostomy, he showed roentgenologic evidence of jejunal ulcer within one month.

SUMMARY—Of these 23 patients with postoperative jejunal ulcer three were female, 20 were male, this ratio approximates the comparative incidence of duodenal ulcer in the two sexes.

In 21 of the 23 cases the original ulcer was in the duodenum. This corresponds with the impression of other authors that patients with duodenal ulcer are more apt to develop jejunal ulcer than those with gastric ulcer.

The interval between gastro-enterostomy and evidence of existence of jejunal ulcer varied from 12 days to 18 years. In seven cases, more than five years elapsed before the first recurrence of digestive symptoms after operation. In nine cases the first roentgenologic evidence of jejunal ulcer appeared from six to 17 years postoperatively. Such figures suggest the fallacy of end-results of gastric surgery based upon five- or even ten-year follow-up.

The Symptoms and Physical Signs of Jejunal Ulcer—In two cases acute perforation, two and 18 years after operation, was the first evidence of existence of a jejunal ulcer. Three other cases also experienced acute perforation, in these, however, antecedent symptoms suggestive of jejunal ulcer had been in existence for two, eight and 12 months respectively.

In discussing the symptoms of jejunal ulcer, as exemplified by these 23 cases, it is essential to remember that jejunal ulcer, like duodenal ulcer, probably begins with superficial ulceration of the mucosa, with or without bleeding from the mucosal vessels. This is followed by penetration into the deeper coats, again with or without bleeding, and finally heals with scar tissue formation. Consequently, different groups of symptoms arise depending upon the state of activity in the ulcer.

The symptoms due to bleeding and cicatricial obstruction did not differ markedly in these cases from symptoms characterizing the same states of activity in duodenal ulcer.

It was in the stage of ulcerative and penetrative activity that the jejunal ulcer gave symptoms markedly different from the original ulcer. In general, the site of pain had shifted from the epigastrium to the umbilical region, and in several cases, even lower, to the hypogastrium. The pain radiated to the left lower quadrant, or left flank, or directly through to the back, corresponding to the segmental innervation of the jejunum. The pain was usually much worse than that of the original ulcer, occurred at more frequent intervals, was more continuous and was less relieved by alkali or food. In one case jejunal ulcer was ushered in by severe thoracic symptoms suggestive of pleural irritation. Several of the patients, with no good evidence for the existence of obstruction, complained of severe "gas" which they had not experienced during corresponding stages of activity in their original ulcers.

With the development of gastrojejunocolic fistula (in one case it was asymptomatic) painless diarrhea developed, later followed by the belching of foul-smelling gas. Fecal vomiting was not observed in any of these cases.

On physical examination abdominal tenderness was elicited a good deal more regularly than with the original ulcer. In general the site of maximum tenderness was localized near the umbilicus, either slightly above or below it, and slightly to the right or left of the midline. In those cases with obstruction the enlarged, dilated stomach or duodenojejunal loop could sometimes be palpated.

The Roentgenologic Diagnosis of Jejunal Ulcer —The roentgenologic signs of jejunal ulcer again depend upon the state of activity of the jejunal ulcer at the time of radiologic examination. The earliest lesions, with only superficial ulceration, may exhibit only tenderness over the stoma or involved segment of jejunum. As the inflammatory process advances, spasm and constriction appear at the site of tenderness. If a considerable number of fluoroscopic examinations are made, the constriction will not appear constantly. This spastic narrowing of the jejunum will frequently disappear if the patient has received sedatives or antispasmodics before examination. With deeper ulceration an actual crater appears. As healing with scar tissue progresses, a real cicatricial obstruction develops which is constant and does not respond to antispasmodics.

In three cases constriction had progressed so far that nothing passed via the stoma, in two instances the obstruction was so marked as to have produced a vicious circle, with barium emptying back into the stomach via the pylorus. Other less frequent signs were marked retraction of the greater curvature above the site of the stoma, exaggeration of the jejunal mucosal folds, overactive peristalsis of the stoma or of the jejunum proximal to the ulcer and marked dilatation of the jejunum above the constriction. In one case, roentgenologic visualization of a gastrojejunocolic fistula was added evidence of the existence of a jejunal ulcer.

It may be remarked, parenthetically, that closure of the gastro-enterostomy stoma does not necessarily mean that the original duodenal ulcer has

healed and that the more natural channel, the pylorus, is being preferentially utilized (Cannon⁴¹), but may be the result of a cicatricial closure of the stoma following jejunal ulcer.

Gastric Acidity in Jejunal Ulcer—Of ten cases which had gastric analyses at the time of development of jejunal ulcer (or shortly before roentgenologic evidence appeared) seven had a moderate hyperacidity, either in the fasting contents or in response to a food test meal, two showed a normal acidity and one showed an anacidity (in the one analysis made). It is interesting that this patient had a Roux en Y-resection, followed by jejunal ulcer, which healed under medical therapy and is still asymptomatic, ten years after the operation. It may be that the development of achlorhydria is responsible for her failure to develop another jejunal ulcer.

In five of these cases there was an opportunity to compare the acidity of the gastric contents before operation for duodenal ulcer with the acidity at the time of development of jejunal ulcer. In these cases gastro-enterostomy did not succeed in diminishing the acidity of the gastric juice.

It is unfortunate that only one of the cases in which an entero-enterostomy was combined with a gastro-enterostomy had gastric analyses at the time of the development of the jejunal ulcer. As would be expected, this case showed a marked hyperacidity in the fasting contents as well as after histamine stimulation.

Preoperative Factors Contributory to Jejunal Ulcer Formation *Indications for Surgery*

Duration of Symptoms—Six of the 23 cases were operated upon during their first attack, with antecedent symptoms only one week to three months in duration. In nine of the 23 cases the duration of symptoms was less than eight months.

Duration and Intensity of Medical Treatment—In only three cases is there evidence that medical treatment was adhered to faithfully for an appreciable length of time. Four cases received practically no medical treatment though in no case was operation considered emergent.

Analysis of Symptoms—In three cases (originally operated upon elsewhere) the records of the symptoms prior to operation were insufficient to permit any conclusion as to the indication for operation. In seven cases the preoperative symptoms were characteristic of early ulceration, with no evidence of penetration, uncontrollable bleeding or cicatricial obstruction. In at least one case the symptoms were more suggestive of gallbladder disease, and gastro-enterostomy was performed as a matter of routine, upon finding a gastric ulcer at celiotomy.

Of the remaining 12 cases the symptoms suggested penetration alone in two cases, penetration and some degree of obstruction in four cases, and obstruction alone in six cases.

Seven of the ten cases in which some degree of obstruction was suggested

by the symptoms showed definite retention upon roentgenologic examination. Of these ten cases, five had gastric analyses before operation and four showed definite hyperacidity.

In no instance in which obstruction was considered the indication for operation had belladonna (or other antispasmodic) been given a prolonged trial preoperatively. The importance of this is illustrated by Case 3 upon whom gastro-enterostomy was originally performed because of obstruction. The patient subsequently developed a jejunal ulcer and the anastomosis was taken down. Shortly thereafter the original ulcer became reactivated and evidence of obstruction recurred. This time, however, the obstruction responded excellently to large doses of belladonna and gastric lavage. If obstruction be the indication for operation, it is essential to evaluate by lavage, antispasmodics and sedatives how much of the obstruction is cicatricial and how much due to spasm and edema.

Operative Factors Contributory to Development of Jejunal Ulcer

Anterior, Long-Loop Gastro-Enterostomy—In three cases the original operation was an anterior, long-loop gastro-enterostomy. In two of these entero-enterostomy or Roux en Y drainage was established at the same time. One of these cases had a recurrence of severe digestive symptoms three weeks after operation, and two months later showed definite roentgenologic evidence of jejunal ulcer. The second case went for three years before developing roentgenologic evidence of jejunal ulcer. The ulcer subsequently healed under medical therapy and the patient is still well, ten years after the original operation. The failure of this patient to develop another jejunal ulcer may be due to the fact that partial resection was performed at the time of Roux en Y anastomosis, or possibly to the development of an achlorhydria (her gastric contents having been found anacid on one examination). The third patient, who did not have a simultaneous entero-enterostomy performed, went eighteen years before suddenly perforating a jejunal ulcer. At this time he was operated upon with Roux en Y technic, despite which he has gone for seven years without a recurrence. This may be attributable to the fact that his original ulcer was gastric, supporting the hypothesis that jejunal ulcer is less apt to occur in patients with gastric ulcer.

Three other cases with jejunal ulcers following previous gastro-enterostomy were reoperated and an anterior, long-loop gastro-enterostomy with an entero-enterostomy established. *These three cases developed jejunal ulcer in six months, three and one-half weeks and twelve days respectively.* Entero-enterostomy by preventing adequate neutralization of gastric acidity is dangerous, when combined with anterior gastro-enterostomy, so that a more vulnerable loop of jejunum is exposed to highly acid gastric juice, it is even more so.

Entero-Enterostomy or a Roux en Y Anastomosis—In nine of the 23 cases entero-enterostomy or Roux en Y anastomosis was the procedure employed. Four of the cases received this type of anastomosis at the time of the operation for the original ulcer. Three of these developed jejunal ulcer in three weeks, ten months and six months respectively. The fourth case had

a partial gastrectomy at the same time and went three years before developing jejunal ulcer

In five other cases entero-enterostomy was established at a subsequent operation for jejunal ulcer. *Four of these developed their second jejunal ulcer in one month, six months, three and one-half weeks and six months respectively. These same patients had gone for two years, two and one-half years, one year and seven years respectively, before developing jejunal ulcer after their first operation, which in no instance included entero-enterostomy.*

One of these cases came to operation a second time for jejunal ulcer. The entero-enterostomy was left *in situ* but a slightly lower loop of jejunum was anastomosed to the stomach. This time evidence of jejunal ulcer appeared in three months. At the third operation for the jejunal ulcer an anterior gastro-enterostomy using a much lower loop of jejunum, combined with entero-enterostomy, was performed. In twelve days highly acid juice was discharging through a jejunal fistula which had perforated through the abdominal wall. This indicates the danger of anastomosing the stomach to low loops of jejunum and of performing entero-enterostomy or other procedures deviating neutralizing alkaline juices from the gastro-enterostomy stoma.

Gastrectomy as a Protection Against Jejunal Ulcer—In three cases partial gastrectomy was performed as the original operation for duodenal ulcer. In two of these cases the resection was of the Billroth II type. These two developed jejunal ulcer two and four years after operation respectively. In the third case a Roux en Y anastomosis was established in addition to the resection, and jejunal ulcer developed three years postoperatively.

Four other cases which had developed jejunal ulcer following gastro-enterostomy later underwent gastric resection. In one of these the operation was a Polya type of resection, and the patient is free of symptoms, six years later. In the second of these four cases a Billroth II gastrectomy was performed and within three and one-half months the patient died of a perforated jejunal ulcer. In the other two cases the Devine type of physiologic exclusion-resection was employed. These two cases should really not be considered as gastrectomies, inasmuch as no actual gastric tissue is removed in this operation. The unusual rapidity with which jejunal ulcer followed exclusion-resection in these cases (three and one-half weeks and 12 days respectively) was undoubtedly attributable to the simultaneous establishment of entero-enterostomy.

It is not intended to discuss here the relative advantages or disadvantages of gastrectomy, but at least in this small group of cases it did not render the patients immune to the later development of jejunal ulcer.

Unabsorbable Suture Material—In only one case was there reason to believe that unabsorbed suture material might have contributed to the development of jejunal ulcer. In three other cases unabsorbable suture material had been used for the seromuscular stitch, but there was no later opportunity to examine the stoma.

Appendix—In five cases the appendix was removed at the time of gastro-

enterostomy In one of these cases, operated elsewhere, the pathologic report was "chronic appendicitis" In 14 of the 23 cases the appendix was not removed, and in those cases in which the gastro-enterostomy was performed at this hospital, it was reported as presenting no evidence of disease at operation Four patients came to operation for duodenal ulcer despite previous appendectomy In comparing the interval of freedom from symptoms following gastro-enterostomy in the groups with and without appendectomy, no significant differences could be noted Four of the patients who did not have an appendectomy still remain well seven to 11 years after their jejunal ulcers have healed, either medically or by secondary operation One of the cases that did very badly after gastro-enterostomy had undergone an appendectomy three months before gastro-enterostomy With so many factors contributing to the pathogenesis of postoperative jejunal ulcer it is naturally impossible to gain precise information as to the exact rôle played by the appendix From the data in these cases its importance would seem to be minimal and its routine removal at the time of performing gastro-enterostomy of questionable value

Postoperative Factors Contributory to Development of Jejunal Ulcer

Adherence to Diet—In 12 cases there was practically no systematized dieting after operation One patient, operated upon elsewhere, did not receive dietary instructions or precautions upon leaving the hospital Six of the patients who departed from their diets during the first year after operation experienced a return of digestive symptoms suggestive of jejunal ulcer within the same year The only two patients who adhered faithfully to a prescribed diet remained well for 14 and 18 years respectively before developing jejunal ulcer The general impression from a study of the records was that the interval of freedom from digestive symptoms after gastro-enterostomy was proportional to the period of strict adherence to a suitable diet

Alcohol—Alcohol played very little rôle in the development of jejunal ulcer in these 23 cases Most of the patients who had previously enjoyed alcoholic beverages had learned from experience that alcohol and peptic ulcer did not agree In 17 of the cases there was no evidence of any use of alcohol In three cases there were definite statements that alcohol was being habitually consumed in at least moderate quantities Only one patient partook of excessive quantities

Tobacco—Twelve of the 23 patients were smoking at least moderately prior to, or at the time of return of digestive symptoms Some admitted smoking as many as 20, and one patient 30 cigarettes daily The relationship between smoking and recurrence of digestive symptoms need not necessarily have been a direct one The excessive use of tobacco may simply have coincided with periods of increased nervous tension, or may have constituted only one phase of a general departure from ulcer regimen

Latent Foci of Infection—The following were looked for as possible foci of infection Teeth, tonsils, sinuses, hemorrhoids, and the genito-urinary tract In nine cases there were no apparent foci of infection at the time of

the first evidence of jejunal ulcer. The other 14 exhibited one or more potential foci of infection. In no instance, however, were these foci considered important or even contributory factors in the formation of the jejunal ulcer. The evidence concerning the rôle of infection in relation to peptic ulcer is purely speculative and still debatable. However, in view of the mere possibility, that despite our lack of evidence infection may bear even a minimal relation to the development of peptic ulcer, it is worth while eliminating such foci of infection in patients with peptic ulcer.

Healing in Jejunal Ulcer—It is commonly thought, and rightly so, that the existence of a jejunal ulcer is a constant threat to the patient's safety. Jejunal ulcers following anterior gastro-enterostomy have been considered more dangerous because of a tendency to perforate freely into the peritoneal cavity, whereas jejunal ulcers following posterior gastro-enterostomy have been considered more likely to become adherent to the transverse mesocolon and colon, with ultimate establishment of a gastrojejunocolic fistula. These impressions were not necessarily borne out by this study. Of five jejunal ulcers operated upon for perforation, two followed anterior gastro-enterostomy. In one of these free perforation had occurred into the peritoneal cavity. Of the other three cases, following posterior gastro-enterostomy, two had perforated freely into the peritoneal cavity. Gastrojejunocolic fistulae ultimately developed in two cases following posterior gastro-enterostomy. The danger of such complications, perforation and gastrojejunocolic fistula might be considered urgent arguments for early operation in jejunal ulcer. However, four patients have now gone from four to ten years after showing evidence of jejunal ulcer, and remain comfortable, except when they indulge in dietary indiscretions. In four cases rigorous dieting produced roentgenologic evidence of complete healing of the jejunal ulcers. In one of these cases the roentgenologic findings reappeared within two years following departure from a suitable diet. The fact that jejunal ulcers like duodenal ulcers may undergo periods of activity and quiescence suggests that if fluoroscopic examinations were made with every return of digestive symptoms following gastro-enterostomy, the incidence of jejunal ulcers might be far greater than is commonly supposed. The fact that jejunal ulcers may heal spontaneously calls for the institution of vigorous dietary measures with alkali, and antispasmodics if necessary, at the slightest recurrence of digestive symptoms.

The Rôle of the Nervous System in Postoperative Jejunal Ulcer—The importance of mental trauma, emotional upset, the stress and strain of civilized life have long been known to be among the underlying causes of the development of peptic ulcers. Ivy lamented the fact that dogs do not worry about the stock market and hence are highly refractory to the development of experimental peptic ulcers. Volumes have been written on the importance of psychogenic and environmental factors in this disease, and the reader is referred to an excellent summary on the subject by Cushing.⁴²

It was evident that most of these patients either had a good deal to worry about, or were the type to worry a good deal over very little. It is difficult

to compare the environmental factors operating at the time of the formation of the original peptic ulcer with those in existence at the time of development of a jejunal ulcer, and only very general impressions may be obtained. These point to the existence of intricate psychologic and sociologic problems deserving of most thorough study.

Prophylaxis and Therapy of Jejunal Ulcer—It is obvious that the best treatment of jejunal ulcer is its prevention. This does not necessarily mean performing less gastric surgery. The fact that only 23 cases of postoperative jejunal ulcer could be found in the files of the Presbyterian Hospital is, in itself, a recommendation for gastric surgery. This, of course, with the reservation that absolute indications for surgical intervention must exist. Unwillingness to adhere to medical measures does not constitute an indication for operation. Since gastro-enterostomy entails at least a temporary period of dieting postoperatively, patients who have not adhered faithfully to medical measures are apt to do badly. As for choice of surgical procedure, entero-enterostomy, a Roux en Y anastomosis, or other procedure resulting in the deviation of the alkaline juices from the site of the gastrojejunoanastomosis should be avoided. Since the small intestine becomes increasingly vulnerable to the corrosive effect of gastric juice, the greater the distance from the pylorus, a jejunal loop as close to the ligament of Treitz as is consistent with a good anatomic result should be selected. If the appendix appears diseased it should be removed. The patient should be properly informed of the importance of dietary measures after operation, and should be especially warned to return to the most rigorous type of ulcer regimen with the slightest recurrence of symptoms. Tobacco and alcohol should be forbidden. Foci of infection should be eradicated preferably before operation. And if, despite such precautions jejunal ulcer should still develop, immediate vigorous medical therapy should be resumed, surgery being reserved for the late complications of jejunal ulcer, namely, perforation, gastrojejuno-colic fistula, uncontrollable bleeding and cicatricial obstruction. If, on the other hand, the original indications for operation were at all questionable, or if an unphysiologic type of anastomosis was employed, a surgical revision is indicated, with dissolution of the gastro-enterostomy or entero-enterostomy.

The confidence of the patient must be gained by a skillful psychotherapeutic approach and his life so regulated, even to the point of altering his environment, as to eliminate tangible sources of emotional disturbance.

CONCLUSIONS

(1) Twenty-three cases of jejunal ulcer following operations for peptic ulcer have been studied. Nine of these had their primary operation for peptic ulcer elsewhere.

(2) Jejunal ulcer occurred more frequently in males in this series.

(3) Jejunal ulcer occurred more often in patients operated upon for duodenal ulcer.

(4) The interval between gastro-enterostomy and the development of

jejunal ulcer varied considerably, the shortest being 12 days and the longest 18 years

(5) The symptoms, physical signs, roentgenologic diagnosis and chemistry of the gastric contents in jejunal ulcer are discussed

(6) The indications for gastric surgery must be definite

(7) Entero-enterostomy, Roux en Y anastomosis and other procedures leading to inadequate neutralization of gastric acidity should be avoided

(8) Low loops of jejunum should not be selected (this applies particularly to anterior gastro-enterostomy)

(9) Partial, and even subtotal gastric resection is no guarantee against the future development of jejunal ulcer

(10) The importance of the postoperative regimen is discussed

(11) The importance of the psychotherapeutic approach to ulcer patients is discussed

(12) The prophylaxis and therapy of jejunal ulcer is discussed

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FUSION IN CHARCOT'S DISEASE OF THE KNEE

A NEW TECHNIC FOR ARTHRODESIS

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A TONE of pessimism pervades the surgical literature dealing with arthrodesis for the treatment of Charcot's arthropathy. Because only an occasional successful fusion has been reported, it seems of value to describe an arthrodesis obtained by means of a technic which has not been previously described.

The method consists of a two-stage operation, the object of the primary procedure being to improve the vascular supply of the involved area through extensive multiple drill-holes. The drill should be at least four inches long and one-fourth of an inch in diameter. The technic consists of placing drill-holes in both femoral and tibial condyles in a fan-shaped distribution so that on each side the drill-point penetrates the cortex in the region of the parosteal bone formation, and in the shaft it should travel for three or four inches into the medullary cavity. The leg is then immobilized by a posterior plaster splint for a period of four to six weeks after which time a standard arthrodesis is performed.

It is well known that there is no actual infection and no toxin present at the site of Charcot's disease. The experimental work of Eloesser showed that neuro-arthropathies can be produced by traumatizing the joints of cats in which the limb has been previously rendered anesthetic by severance of the posterior sensory nerve roots. It would appear, therefore, that the underlying pathologic change is the destruction of the normal protective sensory mechanism of the joint so that it is unable to carry on its normal response to trauma. In a typical involvement of the knee there is primarily diminished sensation, followed by marked effusion, distention of the capsule and relaxation of the ligaments. These changes lead to injury of the articular cartilage and to marginal fractures and sprains with extensive formation of loose bodies. Because of lack of normal reparative processes the bones become sclerotic and there is curtailment of the blood supply. Thinning of the articular cartilage leads to further sclerotic changes in the subchondral articulating areas. Sclerosis may also extend several inches from the joint margin. Concurrently with these joint changes there is a luxuriant growth of irregular masses of parosteal bone which seems to be an effort to repair those injuries which extend through bone to the area of the periosteum. Because of the limited regenerative powers and the avascularity of the bones making up these joints, it seemed

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reasonable to attribute the failure of fusion to a lack of suitable bone tissue. The anticipated change produced by the multiple drilling was verified when five weeks after such drilling of the femur and tibia microscopic studies of sections of bone showed new capillary formation and new fibroblasts and osteoblasts in the channel where the drill had penetrated.

Case Report—E. M., Italian, male, age 51, was examined, in 1927, by an internist because of paresthesia of the chest. His blood Wassermann was four plus. Intravenous and intramuscular antiluetic treatment was administered between 1927 and 1929. In 1931, while the patient was receiving weekly intramuscular injections of mercury, he began to



FIG. 1.—Preoperative roentgenograms (April, 1937) of a case of Charcot's disease of the knee joint.

develop discomfort, swelling and instability of the left knee. He was examined by the author at that time and a diagnosis of Charcot joint was made. A Thomas walking-caliper brace was applied which allowed him to get about better, but he found it annoying. In spite of continued antiluetic treatment the deformity and swelling of the knee increased until April, 1937, by which time the patient had become totally disabled because of a marked outward bowing of the knee, and the resulting instability so great that he could not walk satisfactorily (Fig. 1). At that time the spinal fluid showed Wassermann, one plus; Lange, 0012210000. Cell count, 6 per cm. Pressure 180 mm. Blood Wassermann negative. Urine negative.

Operative Procedures—April 19, 1937. Under spinal anesthesia, a median parapatellar incision two inches long was made exposing the knee joint. Fifteen drill-holes were placed radially through both condyles of the femur and tibia with a one-quarter inch drill. The leg was then fixed in a plaster splint. On May 28, 1937, an arthrodesis was performed, employing the following technique. A cup-shaped incision six inches in length was made curving just below the patella. Excessive synovia and the fat pad were removed. About one-quarter of an inch of the tibia and of the femur were excised. The tibial spines were refreshed and left protruding through a notch which had been made in the intercondylar fossa. Fixation of the bones was then produced by the introduction of two Steinman pins.

which entered through the upper end of the tibia and were introduced into the femur, crossing each other. The leg was placed in a plaster hip spica. The fixation pins were removed five weeks after operation.

Subsequent Course—Examination on August 25, 1937, showed clinically that the knee was solid. The spica was removed and a posterior plaster splint applied. On November 23,

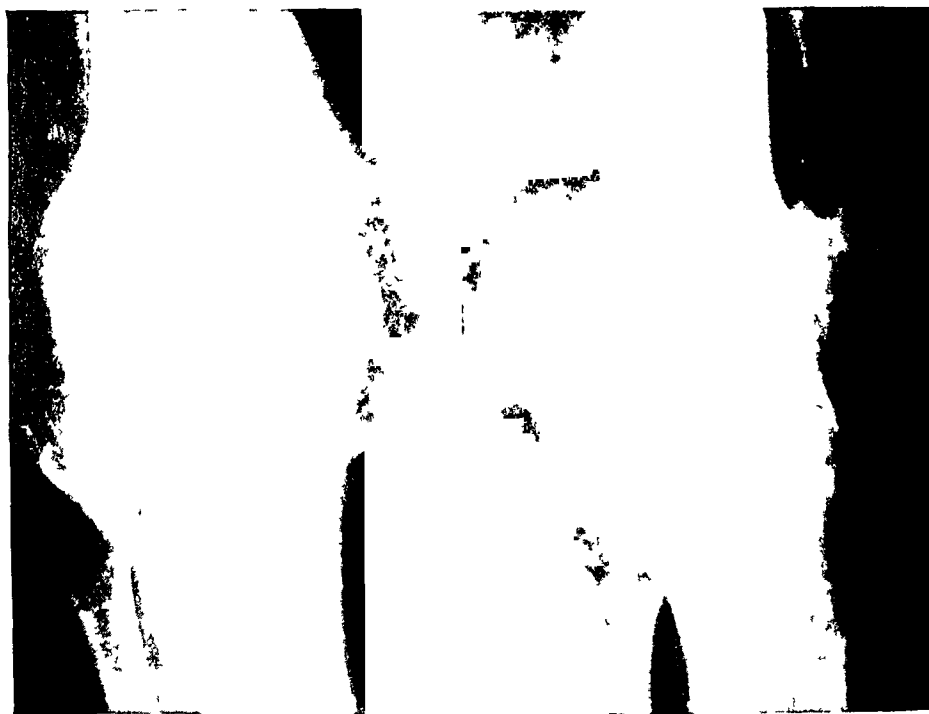


FIG. 2—Roentgenograms (November 2, 1937) showing the result of the arthrodesis five and one half months after operation.

1937, union was present, demonstrated both roentgenologically and clinically, and the patient was allowed free weight-bearing.

SUMMARY AND CONCLUSION

A report is made of a rapid and successful fusion in a case of Charcot's disease of the knee by a two-stage operation, the primary procedure consisting of multiple drilling of the involved bones to increase their vascularity and osteogenic power. This procedure was followed five weeks later by an arthrodesing type of operation.

The results of arthrodeses upon neuropathic knee joints have been disappointing. This may be attributed to the poor blood supply and to the sclerosis of the osseous tissue, rather than to any inherent loss in the processes of tissue reaction and regeneration.

INTRAMEDULLARY PRESSURE WITH PARTICULAR REFERENCE TO MASSIVE DIAPHYSEAL BONE NECROSIS

EXPERIMENTAL OBSERVATIONS

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As a result of Lexer's¹ experimental studies, the anatomic distribution of blood vessels in long bones is now clearly understood. But there has been so little concrete experimental study of the function of these vessels, in the voluminous literature dealing with growth, repair, regeneration, atrophy, necrosis and other disorders of bone, that their fundamental physiologic reactions remain, with few exceptions, unknown.

Axhausen² found focal epiphyseal bone necroses associated with resorption and incomplete repair in embolism of epiphyseal vessels. Although Streptococci were cultivated from these lesions he attributed the degenerative change to ischemia rather than bacteria because of the absence of inflammation.

Nussbaum³ experimentally verified the ischemic nature of the lesions described by Axhausen. Nussbaum's work is of particular interest because it is one of the few dealing with experimental vascular insufficiency of epiphyseal bones.

Muller⁴ observed focal necrosis of compact human bone in advanced arterial sclerosis due, he believed, to infarction. He attributed the brittleness of senile bone to these lesions and emphasized the difficulty of producing prolonged bone ischemia by simple arterial occlusion. In no instance did he encounter medullary necrosis.

The experiments of Johnson⁵ constitute the first fundamental contribution to our knowledge of the rôle played by each of the three components of the blood vascular system of long bones in bone repair. Johnson concluded that outer cortical bone is supplied and its viability maintained by periosteal vessels, whereas the internal portion of the shaft and metaphyses is supplied and kept viable by the nutrient and metaphyseal vessels.

Brunschwig⁶ produced extensive bone and marrow necrosis in experimental animals by actually destroying most of the periosteal, metaphyseal and nutrient vascular connections. In some of his experiments the necrosis involved almost the entire shaft and marrow. Infarction occurred only in animals with unclosed epiphyseal lines, and in no instance was there sequestration.

While Brunschwig had shown that bone and marrow could be killed by extensive interference with their blood supply, Drinker and Drinker⁷ first studied blood flow and cytology of living marrow vessels perfused with dif-

ferent substances at different pressures. They demonstrated the effect of stimulation and interruption of the nerve accompanying the nutrient vessels and the effect of asphyxia on volume flow of blood. Their experiments were conducted, however, under conditions in which collateral circulation of the periosteum and metaphyses was uncontrolled and the state of the epiphyseal cartilages in these experiments is not clearly described.

In 1928, Axhausen⁸ and his collaborators advanced the hypothesis that massive necrosis in acute suppurative osteomyelitis is due to septic infarction of bone.

Phemister⁹ pointed out that the experimental findings of Johnson and Brunschwig are contrary to this assumption because complete ischemia of a massive segment of diaphyseal cortex would require obstruction of at least two independent vascular networks.

We would suggest, however, that the rigidity of the walls of medullary cavities in long bone, and the close interdependence of volume blood flow and pressure which this anatomic characteristic implies, indicates that massive necrosis of acute suppurative osteomyelitis may be due to ischemia caused by increased intramedullary pressure, which may produce its effect independent of the course and origin of the vessels involved. Studies of the effect of pressure exerted in and upon long bones are infrequently recorded in literature.

Beigman,¹⁰ attempting to ascertain the mechanism by which the pressure of expansile tumors produced its changes, drove expanding pins into the medullary cavities of long bones. Spiral fractures always followed. Employing pegs of diameter slightly less than the medullary cavity, he found extensive, painless lacunar resorption, never involving the whole thickness of the shaft, associated with both periosteal and endosteal proliferation, and concluded that continuously acting pressure from inside the medullary canal produces greater proliferation than absorption. One must credit him with clearly emphasizing the importance of distinguishing changes in growing and adult bone, differentiating between directly and indirectly applied pressure, and indicating the importance of the axis of the bone in which pressure is applied. It is almost paradoxical that this investigator, studying pressure which produces its effect so frequently by disturbances in circulation, should have overlooked the importance of the tremendous damage to medullary circulation which his experimental methods induced.

Robl,¹¹ studying the effect of externally applied pressure, wrapped the long bones of rabbits with elastic bands and springs, and produced resorption of a thin layer of underlying cortex, greatest at the site of greatest pressure. He did not ascertain to what extent these changes were due to the immediate injury of the periosteal circulation or its subsequent exclusion.

Burkhardt,¹² applying pressure to the whole extremity by wrapping the legs of rabbits and dogs with elastic bands, found that extensive bone necrosis accompanied soft tissue necrosis, that bone is especially susceptible to disturbances in circulation, that the marrow withstands ischemia better than

the compact bone itself, and that bone proliferation occurs only when the damage has been great enough to involve the marrow. While the degree and duration of circulatory exclusion is not quite clear in his paper, it constitutes one of the first purely physiologic studies of the bone blood vascular system. The simplicity of the experimental method is worthy of mention.

It is the purpose of this paper to record experimental results obtained in the study of intramedullary pressure with particular reference to massive diaphyseal bone necrosis.

Part I Studies of Intramedullary Vascular Pressure

Animals—Ten dogs, young and old adults, were employed. Some of these were street dogs, other had been fed on regular balanced diets with adequate proteins, salts and vitamins for a period of several weeks before being studied.

Preparation—The animals in good health were anesthetized with 0.03 Gm of barbital per kilo intravenously. They were then given 200 mg Toronto heparin intravenously. The right common carotid was cannulated low in the neck and after shaving and preparing the left thigh, the distal one-eighth of the femoral shaft was exposed without otherwise disturbing the periosteum or its adjacent and contiguous structures.

Procedure—The periosteum over the anterior surface of the femur was then incised vertically for approximately 2.5 cm, the central portion of the incised periosteum stripped laterally about 0.5 cm on each side, and the cortex of the femur was then perforated approximately 2 cm proximal to its distal epiphysis by a 0.75 cm drill. The marrow was punctured by the perforating drill as it penetrated the cortex. A tapered threaded steel cannula was then turned into the cortical perforation, immediately connected to a mercury manometer, and the pressure, thus obtained, recorded simultaneously with the right carotid arterial pressure on a common base line.

Results—In eight dogs the marrow cannula pressure obtained in this manner rapidly rose to 30 to 40 Mm of mercury. Pressure variations in the medullary system occurred simultaneously with carotid arterial pressure variations but were of less magnitude. Even Traube-Hering type variations in pressure could be clearly seen in the medullary cannula system. These pressure relationships persisted for the duration of the life of the animal if anticoagulants were repeatedly administered.

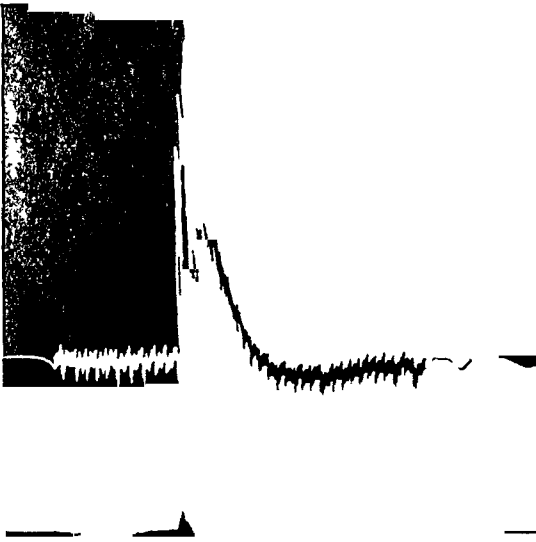
In two dogs the medullary pressure did not rise. In one a clot was found about the bur-hole. In the other the cannula had probably been screwed against the opposite wall.

Conclusions Part I—When dogs anesthetized with barbital are heparinized and the marrow cavity cannulated in the manner described, the average relationship of arterial to intramedullary cannula pressure is approximately 3:1 and the intramedullary cannula pressure changes parallel the arterial pressure variations.

Part II Studies of the Effects of Adrenalin, Ephedrine, Pituitrin and Histamine on Intramedullary Pressure

Adrenalin Hydrochloride—Experiment Eight animals, prepared and anesthetized as in Part I, were each given one-half minims of $\frac{1}{1000}$ adrenalin hydrochloride per kilo intravenously

Results—In all experiments performed, the following of which is illustrative (Graph 1), essentially the same results were obtained Synchronous



with the rise in arterial tension to 200 plus Mm mercury, there was a rise of 4 to 6 Mm of mercury in the intramedullary cannula pressure of only a few seconds' duration, after which the intramedullary cannula pressure precipitously fell from 38 Mm of mercury to 12 to 14 Mm mercury where it remained during the period of elevated carotid arterial pressure Thereafter as the arterial tension fell from 180 to 200 Mm mercury toward normal, the intramedullary cannula pressure gradually rose so that both the arterial and intramedullary pressures returned to their respective levels which they maintained prior to the administration of adrenalin at the same time There was no tendency to a delayed over-rise in the intramedullary cannula pressure

Pituitrin (Surgical)—Experiment Eight animals, prepared and anesthetized as in Part I, were each

GRAPH 1—Adrenalin The upper tracing is the mercury manometer carotid artery pressure The middle tracing is the mercury manometer medullary cavity pressure The lowest tracing is the base line Initial arterial pressure 104 initial intramedullary cannula pressure 34 Mm mercury Ten seconds before the point of the abrupt rise in arterial pressure one-half minims per kilo $\frac{1}{1000}$ adrenalin chloride was given intravenously left jugular Duration of this experiment approximately 20 minutes Note the abrupt and marked divergence of arterial and intramedullary cannula pressure

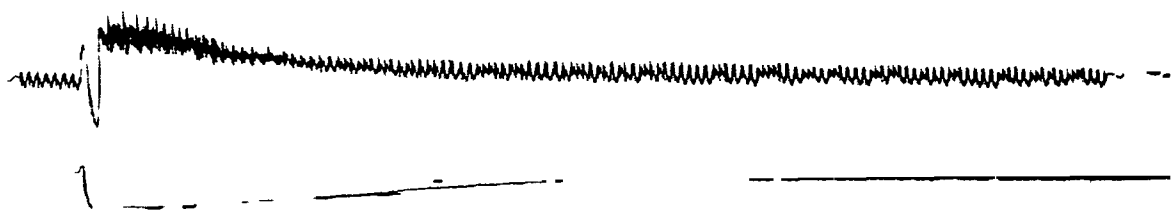
given one unit per kilo pituitrin S, intravenously

Results—In all of our experiments we obtained essentially the same results as in the following graphically illustrated experiment (Graph 2) Synchronous with the rise in arterial tension from 110–120 to 160 Mm mercury, there was a very brief rise in intramedullary pressure of 2 to 4 Mm of mercury followed by an almost instantaneous drop from 36 to 8–10 Mm mercury Coincident with the gradual fall in arterial pressure toward normal there was a slow proportionate recovery rise in intramedullary cannula pressure, both arterial and intramedullary cannula pressure arriving simultaneously at the level maintained prior to the administration of pituitrin

Ephedrine Hydrochloride—Experiment Four animals, prepared and

anesthetized as in Part I, were each given 2.5 mg per kilo ephedrine hydrochloride intravenously

Results—The following graphically illustrated experiment (Graph 3) is typical of the results obtained in all dogs studied. Synchronous with the rise in arterial tension from 110–120 to 180 Mm mercury there was a rise in intramedullary pressure from 34–36 to 52–54 Mm mercury. This relationship persisted throughout the effective period of the drug so that both the arterial and intramedullary cannula pressure reached the level sustained prior to the administration of ephedrine simultaneously.



GRAPH 2—Pituitrin. The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the medullary cavity pressure. The lowest tracing is the base line. Initial arterial pressure 104. Initial intramedullary cannula pressure 36. Ten seconds before the primary rise in arterial pressure one unit per kilo, pituitrin S, was administered intravenously left jugular. The transitory rise in intramedullary cannula pressure followed by the precipitous fall sustained throughout the period of hypertension is apparent. Duration of recorded experiment approximately one hour.

Histamine—Experiment. Four animals, prepared and anesthetized as in Part I, were each given 0.05 mg per kilo histamine hydrochloride intravenously.



GRAPH 3—Ephedrine. The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the mercury manometer intramedullary cannula pressure. The lowest tracing is the base line. Initial arterial pressure 100. Initial intramedullary cannula pressure 38. Ten seconds before the abrupt rise in arterial pressure dog was given 2.5 mg per kilo ephedrine hydrochloride intravenous left jugular. The precipitous sustained rise in intramedullary cannula pressure throughout the period of hypertension is apparent. Duration of recorded experiment approximately one hour.

Results—The results in all dogs studied were almost identical with the following graphically illustrated experiment (Graph 4). Coincident with the abrupt fall of arterial pressure from 120 to 30 Mm mercury there was an abrupt fall in intramedullary pressure from 34 to 24 Mm mercury, widely disproportionate to the fall in arterial tension. Inconstantly present was a short lived secondary rise in intramedullary pressure after the initial decline.

Comparison of the Pressure Effects of Adrenalin, Ephedrine and Pituitrin S—Graph 5 is an illustration of the divergent effect of both adrenalin and pituitrin between carotid arterial and intramedullary cannula pressure, contrasted with the parallel effect of both ephedrine and histamine on these pressures

Conclusions Part II—In animals prepared as described in these experiments, the clear-cut, constant divergent effect produced by both adrenalin and pituitrin between arterial and intramedullary cannula pressure and the parallel effect of ephedrine on these pressures are clearly established

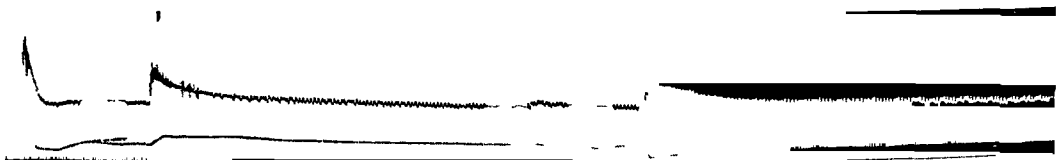
It is not within the scope of this paper to investigate the minute physiologic and pharmacologic reactions which underlie these clear-cut results

GRAPH 4—Histamine The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the mercury manometer intramedullary cannula pressure. The lowest tracing is the base line. Initial arterial pressure 106. Initial intramedullary cannula pressure 38. Eight seconds before precipitous fall in arterial pressure dog was given 0.05 mg. kilo histamine hydrochloride intravenous left jugular. The precipitous fall in intramedullary cannula pressure and its gradual recovery are apparent. Duration experiment approximately 25 minutes.

continuity with the intramedullary vascular pressure, and the results obtained are in accord with what one would anticipate when dealing with a vascular network enclosed in rigid walls

Part III Studies of Degenerative Changes Occurring in Long Bone Following Elevation of Intramedullary Pressure by Physiologic Saline Solution

Experimental Procedure—Part A Dogs and pups ranging from 7 to 14 kilos were deeply anesthetized with barbitol 25 mg per kilo, and the anesthesia maintained by repetition of one-half the above dosage of barbitol



GRAPH 5—Shows the results of a composite experiment in which drugs were given in sequence—producing their characteristic change in intramedullary cannula pressure. The precipitous fall and slow rise with adrenalin and pituitrin is in interesting contrast to the sustained rise produced with ephedrine. (a) Adrenalin (b) Ephedrine (c) Pituitrin S

supported by $\frac{1}{4}$ G1 morphia whenever the animals reacted sufficiently to whine or move

DIAPHYSEAL BONE NECROSIS

TABLE I

GROUP I—BUR-HOLE IN SHAFT OF BONE

Hydrostatic Pressure of 65 to 75 Cm

Dog No	Hydrostatic Pressure in Cm	Length of Time Pressure Was Applied	Number of Cc Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
4	65	22 hrs	15 (clot in cannula)	24 hrs	Dog did not recover from anesthetic There was no edema or separation of periosteum
2	65	22 hrs	400 (clot in cannula)	36 hrs	Dog did not recover from anesthetic There was no edema or separation of the periosteum
15	65	24 hrs	400	19 days	On fifth postoperative day wound spontaneously partially disrupted, drained sanguinoseropurulent material 4 days, then gradually healed over Killed on nineteenth day There was an irregular thin layer of periosteal new bone deposited over distal half of shaft, the underlying cortical bone was grossly normal and the marrow in the distal half was gray Epiphyseal cartilages grossly normal
14	65	48 hrs	2,000	23 days	On sixth postoperative day wound spontaneously disrupted, discharged serosanguineous material for 6 days, then gradually closed Killed on twenty-third day There was slight thickening of periosteum around bur-hole Cortical bone grossly normal Marrow in immediate vicinity of bur-hole grayish, amorphous, surrounded by plug of granulation tissue Epiphyseal cartilages normal
101	70	20 hrs	2,650	7 days	No separation of wound although on third day considerable swelling of soft tissues of entire thigh Killed on seventh day Periosteum slightly thickened, easily stripped No gross defect in cortical bone Bur-hole marrow defect filled with vascular granulation tissue Epiphyseal lines closed Epiphyses normal

Operative Procedure—The animals were well padded and their restraints loosely applied The entire thigh and leg were shaved and cleaned and a lateral vertical incision made over the lateral intermuscular septum, the muscles were separated at the septum and two inches of the distal femur

exposed. The lateral periosteum was then incised vertically 3 cm, stripped laterally 0.5 cm at the midpart of the incision and the underlying cortex was then perforated by a 0.75 cm drill. The underlying marrow was penetrated as the drill slipped through the cortical bone. A phlegmated screw cannula was then turned into the medullary cavity. A pressure apparatus supplying sterile salt solution, 0.9 per cent, was then coupled to the cannula and the wound in muscle, fascia and skin closed with interrupted silk. No attempt was made to close the periosteum.

At the termination of the experiment, the pressure for the first time was lowered or discontinued and the cannula removed. A single skin suture previously placed at the site of the emergence of the cannula was then tied. Collodion dressing was applied and the dog allowed up without splints.

TABLE II
Hydrostatic Pressure of 105 to 135 Cm

Dog No	Hydrostatic Pressure in Cm	Length of Time Pressure Was Applied	Number of Cc Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
30	105	24 hrs	350	10 days	No separation of wound although from third to seventh day thigh was extremely swollen. Killed on tenth day. There was diffuse thickening of very vascular, normally adherent periosteum, beneath which there was widespread deposit of new bone intimately adherent to old shaft which when separated from the subperiosteal bone was irregular and moth-eaten on the opposing surface. There was an area of white bare bone about 2 cm long on each side of the bur-hole. Marrow irregularly soft, homogeneous, yellow throughout canal. Epiphysis closed, no gross abnormality.
34	135	23 hrs	6,600	10 days	On fifth postoperative day wound opened spontaneously, drained large amount of purulent material and was granulating. Draining when animal was killed on tenth day. There was diffuse thickening of very vascular periosteum which formed part of the wall of a large extraperiosteal abscess. Diffuse deposit of large amount of subperiosteal new bone intimately continuous with bone of old shaft from which it could be peeled leaving rough mottled surface. Small area bare yellow bone immediate vicinity bur-hole. Marrow irregularly necrotic. Epiphysis closed, no gross abnormality.

DIAPHYSEAL BONE NECROSIS

TABLE III
Hydrostatic Pressure of 180 Cm

Dog No	Hydrostatic Pressure in Cm	Length of Time Pressure Was Applied	Number of Cc Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
80*	180	12 hrs	400	14 days	Wound did not disrupt On fourteenth day when killed there was massive sequestration of distal one-third of shaft, from which the periosteum was separated by a large amount of thin purulent fluid, complete separation from the distal epiphysis and diffuse deposit of new bone over cortex of upper two thirds of shaft, beneath which old cortex was rough but in intimate continuity with newly deposited bone Marrow totally necrotic in distal one-third, irregularly necrotic mid shaft, and red near upper metaphysis
117*	180	22 hrs	2,100	16 days	Wound remained closed Marked swelling and redness until sixth postoperative day Killed on sixteenth day Distal one-third of shaft except in immediate vicinity of epiphysis bare and white Periosteum elevated and separated from dead bone by pus Epiphyseal line closed No separation General deposit new firmly adherent subperiosteal bone remainder of shaft Marrow necrotic except in spongy bone adjacent to epiphysis
114*	180	20 hrs	3,400	12 days	Wound healed without disruption Killed twelfth day Complete sequestration shaft with separation of periosteum by subperiosteal pus and separation distal epiphysis
47	180	24 hrs	No appreciable infusion	18 days	Wound infected Drained very little Killed on eighteenth day No bare bone save in immediate vicinity of bur-hole, filled with granulation extending into marrow which was widely necrotic and amorphous Extensive thinning of old cortical bone by granulation tissue in marrow and deposit of new layer of subperiosteal bone thicker than the original diaphysis Epiphyseal lines closed and there was marked absorption of end of shaft adjacent, which was replaced by cancellous bone from the epiphysis partly obliterating the distal marrow space

* Mixed flora including *Staphylococcus aureus* obtained from subperiosteal fluid of animals 80, 117 and 114

TABLE IV
Hydrostatic Pressure of 240 to 265 Cm

Dog No	Hydrostatic Pressure in Cm	Length of Time Pressure Was Applied	Number of Cc Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
46	256	24 hrs	? but infusion took place	8 days	Died Extensive necrosis of bone with separation of both epiphyses and denuded lower one-third of shaft <i>Grossly infected</i> During 8 of the 24 hours of pressure, tap water was used
37A	240	20 hrs	1,500	12 days	Marked swelling of thigh from second to sixth day when wound broke open and drained small amount for 3 days Killed on twelfth day Entire shaft bare except small area of attachment (?) at linea aspera and at metaphyses, where the periosteum for approximately 1 cm was adherent to the underlying epiphysis and resorbing shaft through a layer of new bone 0.5 cm thick A clear-cut line of separation between the shaft and epiphysis was clearly demonstrable at the cortex but the medulla for approximately 2 cm was replaced by dense cancellous bone continuous with the epiphyseal bone and new subperiosteal bone deposits The periosteum itself was greatly thickened and extremely vascular It contained new bone only where directly approximated to dead shaft near the metaphyses and along the linea aspera
6	265	8 hrs	?	37 days	Killed on thirty-seventh day There is tremendous enlargement of the entire shaft When bisected the thickening is found due to tremendous, diffuse deposit of new, dense subperiosteal bone The outline of the old shaft is very irregular both on periosteal and endosteal sides It, in places almost invisible, is still present at the midshaft but near the epiphysis is obliterated by new bone The marrow cavity is entirely filled with dense spongy bone directly continuous with epiphyseal bone and subperiosteal new bone
73	180	12 hrs	2,900	11 days	Wound grossly infected from onset Killed eleventh postoperative day Large abscess involving deep tissues and communicating with separated periosteum Distal one-half of shaft bare Distal epiphysis separated at epiphyseal line

DIAPHYSEAL BONE NECROSIS

Part B In this series the same anesthetic and preparation were employed as in animals in Part A The marrow was cannulated by exposing the femoral condyles and perforating the epiphysis and metaphysis Pressure was applied as in Part A, and at the termination of the experiment the cannula was removed and the drill hole plugged with wax and fascia The joint capsule and skin were then closed with interrupted silk

TABLE V
GROUP 2 —BUR-HOLE IN INTERCONDYLAR REGION
Hydrostatic Pressure of 180 Cm

Dog No	Hydro-static Pressure in Cm	Length of Time Pressure Was Applied	Number of Cc Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
3	180	24 hrs	4,000	7 days	Killed Extensive necrosis of entire shaft Complete separation periosteum from shaft
6	180	32 hrs	? but infusion took place	9 days	Died Extensive necrosis of left femur Separation of epiphyses and periosteum Large accumulation of subperiosteal pus
17	180	24 hrs	? but infusion took place	5 days	Killed Specimen discarded No bone necrosis or periosteal change Bur against opposite wall?
37B	180	24 hrs	Only small amount	10 days	Killed Periosteal thickening No resorption No separation of epiphysis Plug of compressed marrow and blood at mid-part of marrow canal This may have occluded the cannula
2	180	24 hrs	? but infusion took place	7 days	Killed Extensive separation periosteum from distal one-half of shaft No separation epiphysis Marrow widely destroyed by cannula

Summary Part III—When the femoral marrow cavity is infused with physiologic salt solution

(A) At pressures from 65 to 75 cm of salt solution for 20 to 24 hours (Table I)

(1) The amount infused ranges from 400 to 2,650 cc

(2) There is no edema or elevation of periosteum during period of infusion and for 24 hours after ward

(3) The marrow is killed irregularly distal and adjacent to the site of infusion

(4) Sequestration of bone does not occur although the wounds are grossly infected

(5) There occurs a small amount of periosteal new bone especially distal to the site of infusion

(B) At pressures from 105 to 135 cm salt solution for 23 to 24 hours (Table II)

- (1) The amount infused ranges from 350 to 6,600 cc
- (2) The marrow is killed irregularly throughout most of the cavity
- (3) Sequestration of bone occurs only in the immediate vicinity of the site of infusion even though the wound be grossly infected
- (4) Periosteal new bone is deposited throughout the extent of the shaft, and there is resorption of the underlying cortical bone

(C) At pressures of 180 cm or greater salt solution for 12 hours or more (Table III)

- (1) The amount of salt solution infused ranges from 400 to 3,000 cc (Table V)
- (2) The marrow becomes completely necrotic
- (3) Massive necrosis of bone with subsequent separation of periosteum and one or both epiphyses occurs. Because of spontaneous reopening of wounds, as subperiosteal fluid accumulated, all wounds studied ultimately became infected in this series. Mixed flora including *Staphylococcus aureus* were recovered from all wounds studied

(4) Typical involucrum may be formed where sequestration occurs. In two instances (Dogs 6 and 37A, Table IV) sequestration did not occur but a massive segment of old shaft was undergoing substitution when animals were killed.

Conclusions Part III—(1) The medullary infusion of 0.9 per cent salt solution at pressures below 75 cm for 24 to 48 hours does not lead to bone necrosis even though the wounds are grossly infected.

(2) The medullary infusion of 0.9 per cent salt solution at pressures of 180 cm or greater for as short a period as 12 hours, independent of the amount infused, leads to massive bone necrosis, followed by massive sequestration in bones whose epiphyseal cartilage existed at the time of the experiment, and widespread resorption in bones where epiphyseal lines had closed prior to the experiment. All wounds studied bacteriologically in this series ultimately became infected.

(3) The continued infusion of salt solution, the absence of necrosis or substitution in bones exposed to (55 Mm mercury) 75 cm salt solution pressure for 24 hours even when infection follows, and the constant bone substitution or sequestration incurred by application of pressures of (77 Mm mercury) 105 cm salt solution or greater leads us to the conclusion that increased intramedullary pressure may be of extreme importance in the production of massive bone necrosis.

(4) In these experiments "stripping" of the periosteum was not a factor in the production of bone necrosis since the periosteum was incised at operation widely enough to allow of decompression throughout the period required for periosteal detachment to occur. Detachment of periosteum is, therefore, secondary to necrosis of the shaft in these experiments and represents the reaction of the living periosteum to the dead infected bone, rather than a primary factor in the production of massive necrosis.

(5) Our experiments suggest that sequestration of dead bone occurs only when there has been complete destruction and long continued exclusion of the vascular connections between bone and surrounding vascular tissue

DISCUSSION

We are aware that in the experiments cited the marrow cannula fluid was often in continuity with the open marrow vascular system. However, the rapidity with which marrow cannula pressure changes were induced by the drugs administered in Part II as well as the marked variation of fluid infused



FIG 1—A roentgenogram taken 18 days postoperative of an experimental animal whose tibia had been subjected to 160 cm salt solution for 24 hours (For the sake of clearer roentgenographic reproduction, the tibia above, not included in the foregoing experiments was used rather than the femur)



FIG 2—A photograph of a typical specimen of massive necrosis produced by high intramedullary pressure (240 cm) which was removed from Dog 37A, Table IV

in Part III suggest that the degree of open communication between marrow vessels and cannula fluid in these experiments was relatively insignificant

In long bones the total medullary capacity in a given bone is fixed by the inexpandable cortex forming its walls except as it is modified by growth or disease. Moreover, excluding the marrow vessels the medullary cavity is occupied by relatively incompressible material. Intramedullary tension must, therefore, be normally dependent upon intravascular tension. Likewise any increase in the relative volume of extravascular tissue can occur only at the expense of the volume of blood in the vascular bed.

In our pressure experiments, therefore, it would seem that whether the circulation in bone and marrow was excluded by compression of vessels or

by substitution of salt solution by infusion is insignificant. And, while part of the exclusion of the circulatory bed in acute suppurative osteomyelitis is probably due to the accumulation of inflammatory exudate in extravascular tissues of bone and marrow, this process is probably of greater importance in zoning pressure heads within the marrow cavity than in the production of absolute ischemia as indicated by the results of Johnson's⁶ experiments.

In our opinion the results of the foregoing experiments have an extremely important clinical application in the treatment of acute suppurative osteomyelitis.

Since massive sequestration of diaphyseal bone can occur only secondary to massive bone necrosis, and since massive diaphyseal bone necrosis results from ischemia produced primarily by pressure, the fundamental principle in the treatment of acute suppurative osteomyelitis is *the release of pressure in the infected bone* before the bone is killed.

Failure to clearly distinguish between massive necrosis and sequestration of diaphyseal bone, pointed out years ago by Aukhausen,² and so important in our present concept of the pathogenesis of sequestration in suppurative osteomyelitis, is responsible for much of the current disagreement as to methods of treatment of acute suppurative osteomyelitis and infected compound fractures.

Once diaphyseal bone necrosis has occurred in the presence of infection, the surrounding living bone and periosteum detach themselves, and depending upon the degree and duration of vascular exclusion, sequestration inevitably ensues. The problem then becomes one not of dealing with acute osteomyelitis, but of sequestration and chronic osteomyelitis. Obviously, since the amount of sequestration parallels the degree and duration of vascular exclusion from the dead bone, preservation of maximum vascular connection with the injured bone and the earliest possible reapposition of vascular tissue to the dead bone is of the greatest importance in treating this phase of the disease.

In acute suppurative osteomyelitis, it is, therefore, necessary that the involved metaphysis be opened early if massive necrosis and subsequent sequestration are to be avoided.

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THE EFFECT OF THE DIRECT APPLICATION OF COD LIVER OIL UPON THE HEALING OF ULCERS OF THE FEET IN PATIENTS WITH DIABETES MELLITUS

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IN A previous study¹ we found that careful care of the feet of patients with diabetes mellitus decreased the incidence of infection of the feet, improved the condition of the skin and helped in healing the ulcers. In many cases, however, in spite of this treatment, the ulcers failed to heal and constant foot care was necessary to avoid serious infection. It occurred to us that as the tissues of many of these patients were not in an optimum state of nutrition and as vitamin A stimulates the growth of epithelial tissue, that the direct application of cod liver oil might be an effective method of treatment. The healing action of cod liver oil has been reported by several observers who used it in the treatment of wounds, burns, crushing injuries, superficial sores and carbuncles,^{2 to 11} with results that the authors felt pointed to an increased rate of healing. Cod liver oil has also been reported to have a bactericidal power.^{12, 13}

Observations—Two groups of diabetic patients have been studied, one a control group of 11 patients who received routine foot care, consisting of daily foot soaks, thorough drying, and the application of lanolin. This routine foot care was carried on for a period of from one to 32 weeks. The second group consisted of 21 patients who had received routine foot care for a period of from one to 136 weeks when cod liver oil was applied locally to the lesions. These patients may be considered as their own controls during the period prior to the use of cod liver oil. Some of the patients in Group II were also in the control group, but the lesions were at different sites, except in Cases 1, 6, and 17.

The routine foot care used in the Clinic has been described¹. It is administered weekly in the clinic and also daily by the patient at home. When cod liver oil treatment was instituted this foot care was continued, but after drying the feet, gauze saturated with cod liver oil was applied directly to the ulcer and this was kept in place by a noncompressing bandage.

Of the 11 patients in Group I there were four males and seven females. The average age was 59 years. Eight of the patients were on insulin and the average duration of diabetes was 6.7 years. Six had multiple lesions, five required hospitalization.

In Group II all but four of the patients were over 50 years of age. The age in both groups is consistent with previously reported observations¹ in

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TABLE I
EFFECT OF ROUTINE FOOT CARE UPON ULCERS OF EXTREMITIES IN DIABETIC PATIENTS
Group I

Case No	Age Yrs	Sex	Description of Lesion	Effect of Routine Foot Care	Onset of Diabetes	Diet in Grams			Insulin Daily Units	Remarks
						Carb	Prot	Fat		
1	63	F	Ulcer and callus right plantar surface	Improved but unhealed after 13 wks	1932	150	65	85	25	
6	59	F	Corns right and left great toes Ulcer fourth right, left toe	Healed after 25 wks Improved after 8 wks Healed in 3 wks	1927	150	65	70	25	Recurred
8	49	F	Bleb second right toe Ulcer third left toe (distal)	Improved after 22 wks, not healed	1924	180	65	85	None	Not hospitalized
12	50	M	Ulcer stump right foot (postoper)	Improved after 13 wks, did not heal	1927	200	80	100	40	Stump ulcerated again
17	59	M	2 ulcers right leg, 1 lat surface right leg	Healed after 14 wks Unhealed after 28 wks	1936	180	65	85	None	Hospitalized
19	52	M	Ulcer third left toe	Healed after 6 wks	1936	180	70	85	None	Hospitalized
22	65	F	Hemorrhagic corn fifth right toe	Improved after 17 wks	1929	150	65	75	20	Recurred
23	65	F	Corns two, three, five right toes, distal end third left	Healed after 22 and 32 wks, then recurred	1915	180	65	85	35	Hospitalized
24	48	F	Corn fifth right toe	Unhealed after 24 wks	1930	150	65	75	55	Hospitalized
25	88	F	Corn fifth right toe, with cellulitis	Improved after 3 wks	1930	150	65	75	35	Hospitalized
27	46	M	Infected corn fifth left, and left great toe and second Ulcer fourth left toe, and right great toe	Improved Unhealed for 28 wks Improved	1929	175	75	85	30	All lesions but fifth right toe developed during hospital stay All improved but left great toe which showed osteomyelitis Hospitalized

which 81 per cent of the patients with infections or ulcers of the feet were over 50 years of age. Eleven of the patients studied were females and ten were males. The duration of the diabetes varied from one to 17 years. Twelve of the patients required insulin. There were no significant changes in the diet and insulin requirements in the periods before and during cod liver oil therapy, so that these factors did not influence the results. Fifteen of the patients had multiple lesions at the time of this study (Table II). Six of them had to be hospitalized because of the degree of infection present.

Results—In the control group (Table I) the lesions in Case 1 were improved after 13 weeks but healing did not occur. In Case 6 there was improvement and healing of the lesions, but they recurred later. Cases 8, 12 and 17 improved after 22, 13 and 14 weeks respectively. Case 19 developed ulcers of the same size and type simultaneously on the third left and fourth right toes. One ulcer was treated with routine foot care and the other with cod liver oil. The ulcer on the third left toe, not treated with cod liver oil, healed in six weeks, the ulcer on the fourth right toe, treated with cod liver oil locally, healed in three weeks. Cases 22, 23, 24 and 27 either improved somewhat or remained unhealed after 22 to 32 weeks of treatment. Of the 21 lesions in this group three were unhealed, nine improved, one healed completely and eight recurred.

Of the 21 patients treated with cod liver oil (Table II), only one (Case 16) failed to show complete healing. This patient had generalized arteriosclerosis, coronary sclerosis and evidenced mild congestive heart failure. Continued cod liver oil therapy in the hospital failed to heal the ulcer. Another patient (Case 4) did not heal completely after 44 weeks of cod liver oil therapy in the clinic, but healing resulted in four weeks when bed rest was instituted. In Case 19 there were simultaneous ulcers on the right and left foot, of the same size and type. The ulcer on the left foot was not treated with cod liver oil and healed in six weeks. The ulcer on the right foot treated with cod liver oil healed in three weeks. This patient was in the hospital because of a suspected coronary occlusion, and both ulcers were observed daily.

The average time in weeks required for complete healing of the ulcers, in the 20 cases that healed, was 10.1 weeks. The average duration in weeks of these same ulcers, prior to cod liver oil therapy and during a period of routine foot care, was 24 weeks. These patients during the entire period of observation attended the clinic at least biweekly and during the treatment with cod liver oil, weekly. In four cases the ulcers could really be classified as chronic, having existed for more than 78 weeks.

Before cod liver oil therapy was begun photographs of the feet and the ulcers were made of each patient. Following the institution of cod liver oil follow-up photographs were taken at weekly and later at biweekly intervals. As it is obviously impossible to publish all of these photographs, only some of the cases are shown (Cases 2, 3, 4, 8, 9, 10 and 12).

TABLE II
EFFECT OF TOPICAL APPLICATION OF COD LIVER OIL IN ADDITION TO ROUTINE FOOT CARE UPON ULCERS OF EXTREMITIES IN DIABETIC PATIENTS
Group II

Case No	Age Yrs	Sex	Description of Lesion	Duration of Lesion Before C L O † in Weeks	Vascu- lar State	Healing Time After C L O † in Weeks	Onset of Dia- betes	Diet in Grams			Insulin Daily Units	Remarks
								Carb	Prot	Fat		
1	62	F	Ulcers of right foot plantar surface and left great toe	24	Good	8	1932	150	65	85	25	Complete healing with C L O
2	65	F	Ulceration left fourth and fifth toes Corn third right toe Corn third left toe	32 12 4	Good Good Good	14 9 10	1935	225	65	85	45	Complete healing with C L O
3	65	F	Bleb tip of right great toe	3	Fair	2	1932	175	65	85	None	Complete healing with C L O
4	55	M	Ulcer on plantar sur- face of right great toe	?	Good	48	1936	250	65	85	20	Patient was treated in clinic 44 wks Ulcer improved but healing was incomplete Hospitalized and com- plete healing followed in 4 wks
5	62	F	Blebs on second right and left toes	11	Good	4	1929	250	75	85	25	Complete healing with C L O
6	62	F	Corns right and left two three four Plantar callus right and left great toes	11 11 11	Good Good Good	10 15	1927	150	65	70	25	Had corns since 1933 Improved with routine care Started again and markedly improved after C L O Had plantar callus 2 yrs and 8 mos., which im- proved somewhat on routine care but healed with C L O
7	51	M	Corns right four five left fourth	88	Good	12	1933	200	75	85	35	Had corns 88 wks Improved on routine foot care Then used salicylic acid causing severe ulcers Corns healed 12 wks after C L O
8	49	F	Corn on plantar sur- face right great toe	136	Good	17	1924	180	65	85	None	R F C * helped but C L O resulted in healing

[illegible]

*R F C refers to routine foot care

† CLO refers to cod liver oil

CASE 2



Before treatment 9/3/36



3 wks after treatment 9/24/36



14 wks after treatment 12/10/36



1 wk after treatment 9/10/36



10 wks after treatment 11/12/36



21 wks after treatment 1/28/37

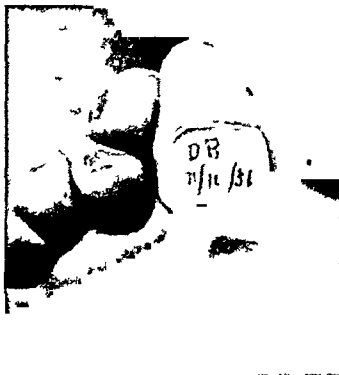
Observing these cases as we did at weekly intervals, it was possible to note the character of the healing that occurred. This healing resulted from a rapid increase in epithelial tissue. As this took place the tissue developed a healthier appearance and the uneven margins smoothed out.

Discussion—The results in Group I are similar to the results obtained in a larger group treated with routine foot care,¹ in which it was shown that the incidence of infection of the lower extremities and the number of cases requiring hospitalization was decreased.

CASE 3



Before treatment 10/29/36



2 wks after treatment
11/12/36



7 wks after treatment
12/10/36



9 wks after treatment
12/24/36



12 wks after treatment
1/14/37



19 wks after treatment
3/4/37

The results in Group II suggest that cod liver oil will increase the rate of healing of ulcers in patients with diabetes mellitus. What factor in cod liver oil is responsible for this remains open to discussion. It may be that the vitamin content is the responsible agent. On the other hand, cod liver oil contains some highly unsaturated fatty acids¹⁴—arachidonic, with an iodine number of 334, and clupanodonic with an iodine number of 368. Unsaturated fatty acids apparently have a stimulating effect on the growth of hair and may also have a stimulating effect on epithelial tissue. We are at present studying the effect of cod liver oil and certain of the unsaturated fatty acids on the healing of wounds in rats rendered chronically vitamin A deficient. The results of these studies will, we hope, throw some light on the comparative effect of these two agents.

CASE 4



Before treatment 8/13/36



8 wks after treatment
10/8/36



13 wks after treatment
11/12/36



16 wks after treatment
12/3/36



26 wks after treatment
2/11/37



29 wks after treatment
3/4/37

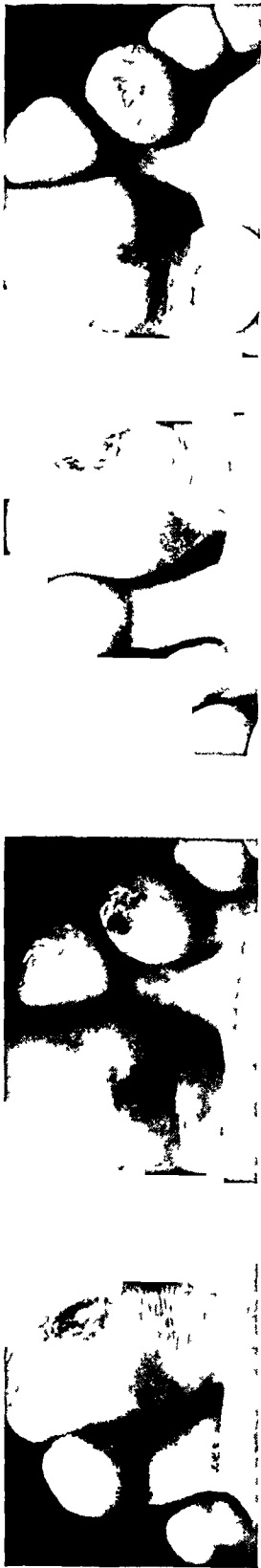


31 wks after treatment
3/18/37



37 wks after treatment
4/29/37

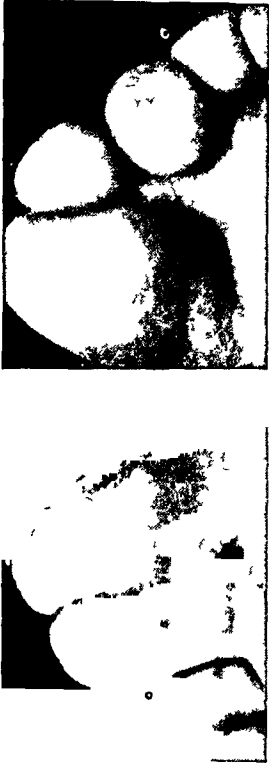
CASE 8



Before treatment 11/12/36

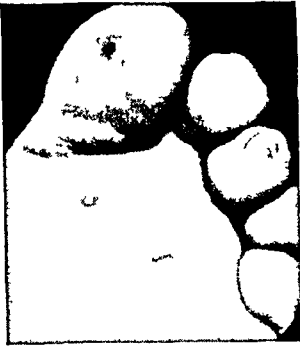


15 wks after treatment 2/25/37



29 wks after treatment 4/29/37

CASE 9



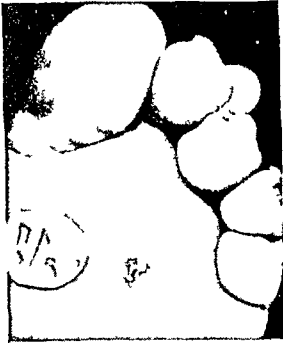
Before treatment 9/3/36



3 wks after treatment
9/24/36



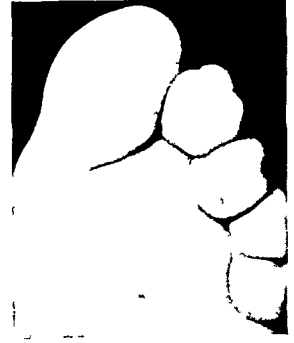
20 wks after treatment
1/14/37



25 wks after treatment
2/18/37



29 wks after treatment
3/18/37



33 wks after treatment
4/15/37

CASE 12



Before treatment 1/21/37



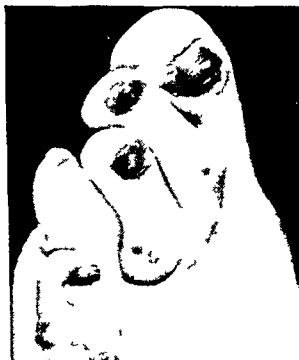
2 wks after treatment
2/4/37



4 wks after treatment
2/18/37



7 wks after treatment
3/11/37



11 wks after treatment
4/8/37



13 wks after treatment
4/22/37

CASE 10



Before treatment 10/1/36



1 wk after treatment
10/8/36



2 wks after treatment
10/15/36



3 wks after treatment
10/22/36



4 wks after treatment
10/29/36



5 wks after treatment
11/5/36



6 wks after treatment
11/12/36



7 wks after treatment
11/19/36

It seems reasonable to suggest, as a result of these observations, that the application of cod liver oil to ulcers occurring in patients with diabetes mellitus will shorten the healing time and so decrease the incidence of infection of the feet

SUMMARY

Eleven diabetic patients with ulcers of the feet treated with routine care were studied for periods of one to 32 weeks. In this group, three lesions remained unhealed, nine were improved, one healed completely and eight recurred.

Twenty-one diabetic patients with ulcers of the feet, which had existed for periods varying from one to 136 weeks, were treated by the topical application of cod liver oil in addition to routine foot care.

All of these patients had been treated with routine foot care prior to cod liver oil therapy.

In 20 of these 21 patients complete healing of the ulcers followed the local application of cod liver oil. The average time required for healing to take place was 10.1 weeks.

The average duration of these ulcers prior to this therapy was 24 weeks.

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BRIEF COMMUNICATIONS AND CASE REPORTS

ACUTE PERFORATION OF A DUODENAL DIVERTICULUM

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FROM THE UNIVERSITY OF KANSAS HOSPITALS KANSAS CITY, KANSAS

Case Report—A white male, age 54, was admitted to the University of Kansas Hospitals, service of Dr Thomas G Orr, April 21, 1937, stating that while at work 22 hours previously he had suffered a sudden severe cramp-like pain in the midabdomen just above the umbilicus. Soon afterward he became nauseated and vomited bile-stained fluid several times. He was taken home in an ambulance and hot and cold packs applied to the abdomen with no amelioration of symptoms. His bowels had not moved during the day and several enemata were given with no return of feces or relief of the pain. About three hours after the onset the low epigastric pain became generalized and remained so thereafter.

The patient denied having had any similar seizures in the past and, in fact, denied ever having had any previous gastro-intestinal symptoms whatever.

Physical Examination revealed a rather poorly nourished middle-aged, white male, apparently acutely ill, lying in bed with thighs flexed complaining of severe generalized abdominal pain. Temperature, 100° F, pulse, 92, respirations, 22, blood pressure, 130/70. The head, neck, and thorax were essentially normal. The abdomen was slightly distended and moved very little with respiration. The entire abdominal wall was tense with board-like rigidity on the right, more marked in the right lower quadrant, where the tenderness was greatest. Hemoglobin, 92 per cent, W B C, 10,000, 84 per cent polymorphonuclears. The blood chemistry was normal.

The patient presented the picture of a ruptured abdominal viscus. An acute appendicitis with perforation was considered to be the most probable diagnosis, although perforation of a peptic ulcer and diverticulitis of the colon with rupture were considered.

Operation—Fibrous adhesions were present between the viscera and the anterior abdominal wall from the region of the pylorus downward into the pelvis. The appendix was thickened and bound down by fibrous adhesions, but no evidences of acute infection were seen. There was free pus in all parts of the peritoneal cavity. Purulent exudate was most marked about the pylorus. The lesser peritoneal cavity was opened and found to contain pus and necrotic tissue. No gastric or intestinal perforation could be identified. The findings, however, suggested a perforation into the lesser peritoneal cavity. The abdomen was closed and drains placed to the lesser peritoneum and right iliac fossa. Cultures from the peritoneal exudate showed *B. coli* and a small gram-positive *Diplococcus*. The patient responded poorly to therapy after operation and died April 24, 1937.

Autopsy—Two duodenal diverticula were found, one on each side of the ampulla of Vater. They were approximately the same size, each measuring about 3 cm in depth by 2 cm in maximum diameter. The diverticulum behind, and to the right of the ampulla, appeared acutely inflamed and had ruptured at its apex into the retroperitoneal tissue behind the head of the pancreas resulting in extensive multiple retroperitoneal abscesses. The infection involved particularly the tissue along the root of the mesentery and about the right kidney and ureter. The ampulla itself showed no gross abnormality.

Submitted for publication October 15, 1937

The only other finding of significance was an extensive bilateral, confluent broncho-pneumonia

COMMENT—Spontaneous rupture of a duodenal diverticulum is apparently a rare occurrence. A search through the English literature on duodenal diverticula revealed a case which was reported in 1926 by Monsarrat¹. This patient, a white female, age 58, gave a long history of "indigestion". A pre-operative diagnosis of acute cholecystitis was made, but at operation a ruptured duodenal diverticulum was found, removed, and the patient recovered.

In 1930, Lucman² also reported a case of a diverticulum of the duodenum which had perforated into the pancreas. The diagnosis was made preoperatively by roentgenologic examination and was confirmed at operation. Recovery, following removal, was uneventful.

Huddy³ reports a case of gangrenous diverticulitis in a white female, age 27, mistaken for an acutely inflamed appendix lying under the liver. At operation a duodenal diverticulum was found, black and necrotic at the tip. The diverticulum was excised and the patient recovered. There may have been some leakage from the diverticulum in this case but no acute perforation was found.

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A MODIFICATION OF THE INCISION FOR THORACOPLASTY*

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NEW YORK, N. Y.

THE PRESENT-DAY operations for thoracoplastic compression of the tuberculous lung differ materially from those of Sauerbruch,¹ Bjaauer² and others,³ beginning about 1908. The first important modification for reducing the gravity of the operation was that of Mauei,⁴ who did not carry his incision higher than the spine of the scapula and still was able to resect the first rib by upward retraction of the skin and mobilization of the deeper tissues. About three and one-half years ago the writer⁵ published a method in which the lower end of the Mauei incision was carried forward in the seventh interspace just below the angle of the scapula. The upper stage of the thoracoplasty was then replaced by the far more valuable apicolysis. Indeed, it has been found that the first rib need not be sacrificed,⁶ provided full compression of the diseased upper lung has been secured. If, then, there are no

* Read before the New York Surgical Society, December 8, 1937. Submitted for publication March 5, 1938.

tuberculous lesions in the lower part of the lung, this apicolytic procedure may be all that is necessary. When, however, there is disease of the lower lung and surgical compression seems advisable, it has been the custom heretofore to reopen the lower part of the first-stage scar and to continue the paravertebral incision downward and outward (Fig 1)

A greatly simplified lower-stage operation is herewith presented, which procedure, apparently, causes the least possible trauma

Since, at the first stage, the seventh rib is within easy reach and the incision has been carried forward around the angle of the scapula, it is unnecessary to reopen this wound. By now incising down upon the ninth or the tenth rib, and retracting the latissimus dorsi and the spinal muscles backward without transversely dividing them, there will be afforded space enough for the completion of the thoracoplasty. Through the incision upon the ninth rib as much of the bone as is necessary may be taken away, just as is usually accomplished in the simple operation for empyema. Then the eighth rib, if still present, may be exposed by retracting upward and the tenth by retracting downward. If it is desired to take the eleventh rib also, the incision may be made upon the tenth instead of the ninth, or still another may be made upon the eleventh rib or in its interspace.

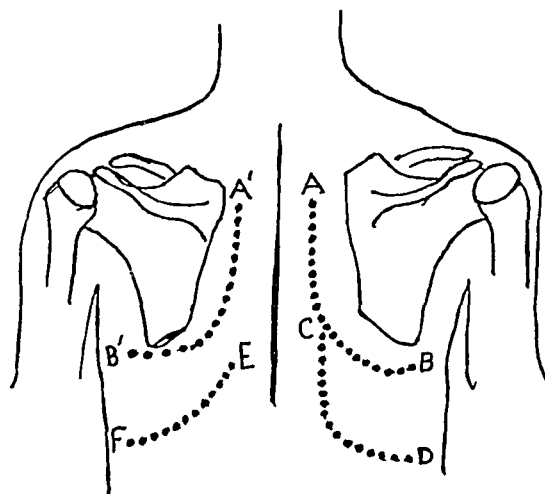


FIG 1—A—B and A'—B' Maurer's incision for upper stage thoracoplasty or for apicolysis (slightly modified). C—D Incision for lower thoracoplasty. E—F Author's incision for lower stage thoracoplasty.

These rib-parallel incisions with muscle retraction, as here described, are far less traumatizing than those which cross the ribs at any angle*. They can nearly always be accomplished under local anesthesia. The postoperative compression is, of course, managed according to the principles for thoracoplasty.

The well-known rule that two shorter wounds are less shocking and less subject to complications than a single long one, holds good in thoracic as well as in abdominal or other surgical procedures.

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* All the usual incisions except that of Maurer are diagrammatically demonstrated in Dr. John Alexander's recent excellent book on collapse therapy.

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DISCUSSION—DR OTTO C PICKHARDT (New York) said that there is as yet no standard incision for thoracoplasty, in the sense that a McBurney, Kammeier, or suprapubic incision is standardized, and, therefore, any new idea is of course welcome. In general, the thoracic surgeon performing a thoracoplasty makes a long curved incision somewhere between the scapula and the spinous processes from above downward, extending it upward for the higher ribs, and downward and forward for the seventh and eighth ribs, around the lower tip of the scapula. This is usually found in the seventh intercostal space. The name "periscapular incision" has been suggested for this. The musculature of the patient and the amount and number of ribs to be resected are, of course, a guide to the length of the cut. The higher the ribs to be resected, the more muscles there are which have to be actually cut across. The lower down the ribs are, the more varied and the easier it is to remove them. The names of Biau, Friedrich, Wilms and Sauerbruch are attached both to their incision and the type of operation. For the eighth, ninth, tenth and eleventh ribs, a hockey-stick type of incision, separate from the first one and placed more medially and lower, is employed. Emile Holman has employed a posterior curved incision added to the lower third of the primary incision. It is in the third and fourth stages, and in the eventual removal of the anterior portions of the unresected ribs that ingenuity must be exercised in order to cause the least possible damage to muscles and nerves.

AN EFFICIENT METHOD FOR THE REDUCTION AND IMMOBILIZATION OF COLLES' FRACTURE^{*}

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BROOKLYN, N Y

TABULATION of the examination of 125 claimants, previously involved in an accident, whose alleged injury was a fracture of the wrist, has shown some interesting facts which have led to changes in our treatment of these fractures. In 102 of these, the examination was made between three and nine months after the accident. More than 75 private physicians, whose names were recorded, and 27 different hospitals rendered the surgical care, so the final results are representative of those now commonly obtained in New York City. The results were good in 82 cases, or two-thirds of the total.

^{*} Read before the New York Surgical Society, October 27, 1937. Submitted for publication September 28, 1937.

COLLES' FRACTURE

Twenty-two had fair results and 21 were poor. Wrist flexion was impaired 20 per cent or more in half of all the cases while extension of the wrist was normal in two-thirds and only a small percentage of restriction was present in the remaining third. Pronation of the wrist was seldom diminished, but supination could not be fully obtained in 22 individuals, or nearly one-

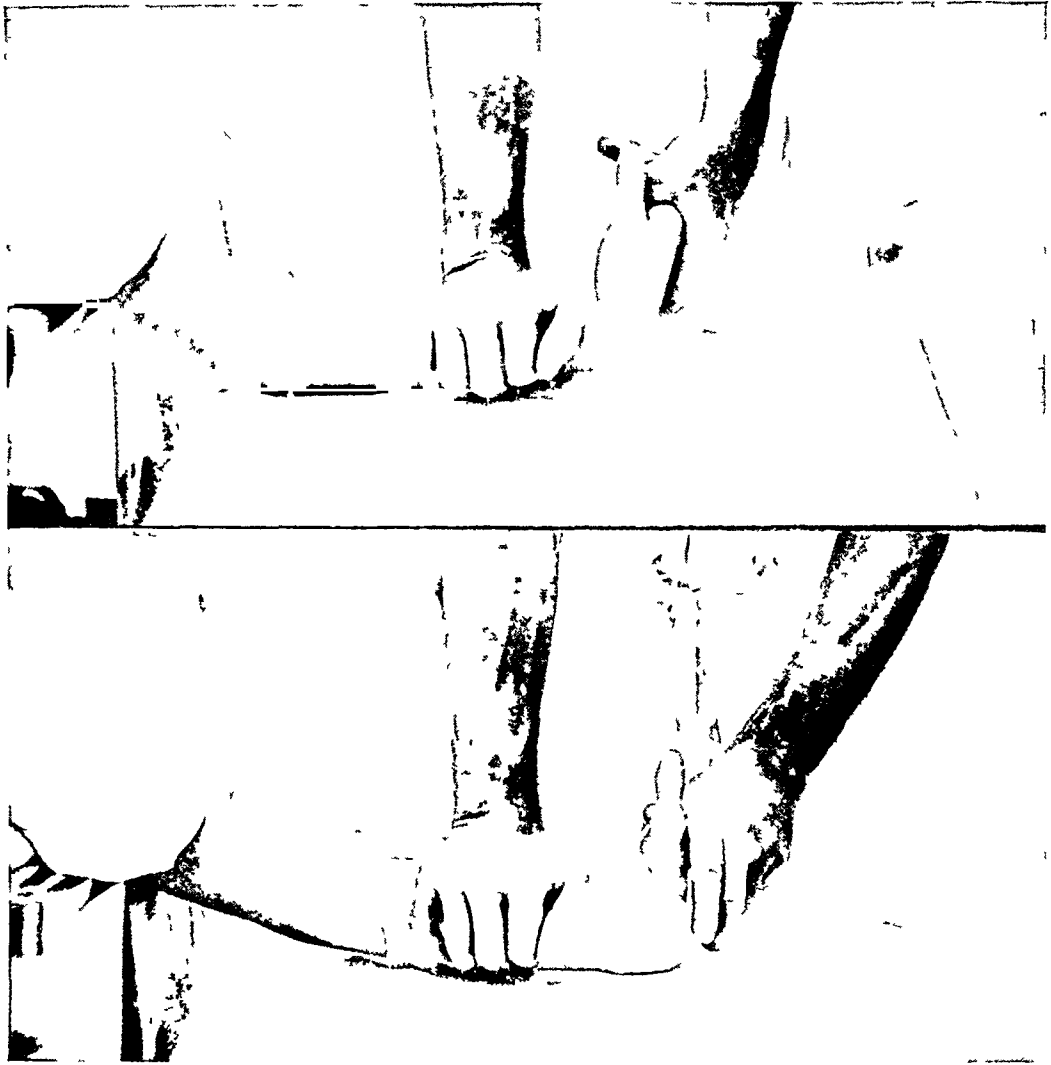


FIG 1—Illustrates the method of reduction
FIG 2—Shows the hand being held in position while the plaster hardens

fifth of the total. Finger flexion was similarly impaired in one-fifth of the cases. Definite deformity, due to anterior displacement of the head of the ulna, was present in 30, and slight deformity in seven others, or nearly one-third of the total. Radial shortening and deviation were found definitely in 27 and slightly in six others, or one-quarter of the total. Failure of a few claimants to prove these fractures in court will merely increase the percentage of unsatisfactory results for the severe injuries need no confirmatory evidence.

To obtain a good result in a Colles' fracture, the first essential is accurate restoration of the displaced bone to its normal position. This is usually attempted by manipulation with the fingers and hands, but is not always successful, for, at times, greater force is necessary.



FIG 3—Shows overcorrection, the lower fragment of the radius being displaced anteriorly



FIG 4—Shows wrist flexion, finger flexion and ulnar deviation with rotation of the hand

FIG 5—Shows wrist flexion and pull on the radius with the fore arm in supination

During the past year we have been using the method shown in Figure 1, which substitutes the push and pull of the strong muscles of the shoulder girdle for the weaker ones of the forearm and hand of the operator. This gives better control of the fragments and more perfect and easy reduction of the fracture. Under anesthesia, with the patient in the dorsal position and the injured upper extremity lying upon a table at a right-angle to the body, the surgeon, who is standing in the angle between the body and the arm, places the forearm in complete supination and rests the base of his palm against the lower end of the upper fragment of the broken radius. With his other hand, he then grasps the hand of the patient, flexes the wrist half way and forcibly pulls the lower end of the broken radius downward and forward as he pushes the upper end backward (Fig 1). A distinct crepitation is usually felt long before the full force available has been used. This indicates a reduction of the dorsally displaced fragment to its proper position. If too much strength is used in this method, an overcorrection or anterior displacement may be produced (Fig 3). This must be carefully avoided.

After proper alignment has been secured, anterior and posterior plaster splints, narrower than the wrist, but thick enough to be strong, are placed in position and the upper ends held by a few turns of a gauze bandage. With the forearm still in complete supination and the wrist in about two-thirds of normal flexion, the bandage is continued downward over the wrist and hand almost to the base of the heads of the metacarpal bones, where the splints should end. Then, while the plaster is still soft, with the wrist thus flexed and held in supination, the hand is pulled away from the radius toward the ulna, making traction on the radius to maintain its full length as much as possible. The hand is also rotated so as to throw the head of the ulna backward. During these manipulations, the other hand of the operator has held the upper portion of the splints firmly back against the table upon which the extremity rests (Fig 2). This position is held until the plaster hardens (Figs 4 and 5). To recapitulate. Complete supination, wrist flexion, hand in ulnar deviation and rotated with the thumb toward the ulna anteriorly.

The fingers and thumb should be flexed and extended from the first day throughout convalescence. The disadvantages of immobilization of the wrist in a flexed position are well known but can easily be prevented by proper care. After one week, the splints should be removed at frequent intervals, the wrist should be firmly grasped by a hand encircling the site of fracture and flexion and extension of the wrist gently performed by the surgeon in ever increasing range as a longer time elapses. The patient should frequently place the forearm in the supine position on a table even while the splints are in place and the sling should be discarded as soon as possible. In a limited number of cases, we have found this an easy method to reduce Colles' fractures and a means of preventing some of the disability and deformity that have followed them in the past. Nothing can take the place of adequate personal attention by the surgeon, and later physical therapy.

The histories of the patients examined show that many of them were kept in splints or in a plaster encasement for a period of six weeks or more with no attempt at regular massage or motion. Undoubtedly, some of the disability and delay in recovery were due to these factors.

An extensive search of the literature has failed to find a description of a similar method for the reduction of Colles' fracture. Buxton¹ says, "Supination is the position of choice in immobilization of fractures of both bones, because it is the optimum position for the recovery of function, as the most important arm movements are from supination to pronation, and after fixation, the latter movement is more easily recovered than supination."

SUMMARY

(1) Examination of 125 individuals at varying intervals after an alleged fracture of the wrist showed impairment of wrist flexion and supination and deformity due to anterior displacement of the head of the ulna and shortening of the radius in a considerable percentage of the cases.

(2) A method previously undescribed, we believe, is proposed for the reduction of Colles' fracture.

(3) A method of immobilization, designed to minimize the disabilities and deformities mentioned above, is described.

(4) The importance of proper care during the period of immobilization is emphasized.

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EDITORIAL ADDRESS

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ALLEN B KANAVEL

1874-1938

THE Editorial Board of the ANNALS OF SURGERY has asked me to prepare a preliminary report of the sudden death of Dr Allen B Kanavel on May 27, 1938, as a result of an automobile accident near his home in Pasadena, Cali-



Photo by Du Bois

ALLEN B KANAVEL, M D

ifornia Doctor Kanavel was a graduate of Northwestern University Medical School in 1896 and served an internship in Cook County Hospital. He then became a member of the surgical faculty of his Alma Mater and advanced gradually to the position of head of the surgical department in which capacity he served for nine years. His success both in the science and the art of surgery was outstanding, and his contributions, especially to the surgery of the hand, gave him an international reputation. He was a member of the staffs of Wesley Memorial and Passavant Hospitals and served from its beginning first as associate editor and then as editor of *Surgery, Gynecology and Obstetrics*. As one of the organizers of the American College of Surgeons, he had an active part in its direction, serving on the Board of Regents for many years and as president in 1931 to 1932. He was elected a member of the American Surgical Association in 1913. In recent years he had resided most of the time in Pasadena.

DALLAS B. PHEMISTER

THE USE OF HEPARIN IN THROMBOSIS*

GORDON D W MURRAY, M D , AND CHARLES H BEST, M D

TORONTO, CAN

THE discovery of heparin in Howell's laboratory, in 1916, and his demonstration that it was a natural anticoagulant of blood, raised hopes that it might also be a preventive of thrombosis. Unfortunately the early experiments on animals and the clinical use of the drug as a preventive of clotting in blood transfusions were discouraging, owing to the toxic symptoms produced. In 1929, however, one of us (C H B) initiated research on the purification of heparin, in the Connaught Laboratories, and Charles and Scott¹ succeeded in preparing it in the form of a crystalline, barium salt, which was 100 times more potent than the original crude material and completely free of toxic properties. This success revived our interest in the possible clinical value of the drug and encouraged us to study, both upon animals and patients, its influence on those pathologic conditions which are based upon thrombosis.

That heparin has a profound influence in preventing thrombosis has been amply demonstrated by a long series of experiments upon animals, begun in the Department of Surgery, in 1932, and reported elsewhere,² in which it was shown that the thrombosis, which normally results from mechanical (Fig 1) and chemical injuries to veins, could be prevented in a high percentage of cases by its intravenous administration. This suggested that, if it could be given safely to patients, it might be used as a prophylactic in those conditions which lead to postoperative pulmonary embolism, and as an adjuvant in those operations upon blood vessels in which the outcome has been so doubtful, because of the tendency of thrombosis to occur at the site of the operation.

Experimental Investigation—The early experiments on toxicity were done on dogs, using heparin of a potency of 15 units per mg. In these animals, when the clotting time had been prolonged to half an hour, muscular weakness and vomiting developed, and when larger doses were given the animals died of profuse intestinal hemorrhage. The postmortem examinations disclosed multiple hemorrhages in all the organs and beneath all serous surfaces. These results led to the efforts to purify heparin and ultimately to the preparation of an extract with a potency of 250 units per mg. This preparation produced no toxic effects on animals even when the clotting time was prolonged to four hours. This encouraged further experimental study.

Arterial Anastomosis—While great improvement has been made in the results of operations on the blood vessels by the development of special technique, there still remains a high percentage of cases in which operations on arteries and veins fail because of thrombosis at the line of suture. In the

* Read before the American Surgical Association, at Atlantic City, N J , May 3, 1938. Submitted for publication June 20, 1938.

hope that heparin might improve the results, a series of experiments was performed in which the axillary, femoral and carotid arteries in dogs were sectioned and then sutured with fine silk. In 50 such experiments, in which regional heparinization was used, the arteries remained patent in 40, or 80 per cent, whereas, when no heparin was used, only 18, or 35 per cent, re-

FIG 1



FIG 2



FIG 1—Illustrating method of inserting the suture before crushing the vein

FIG 2—Anastomosis of artery recovered one year later

mained patent. It was shown in these experiments that, if the lumen could be kept patent for 72 hours, the suture lines were healed and there was no longer a tendency to thrombosis or clotting at this site (Fig 2). Specimens recovered a year afterward showed only a slight scar.

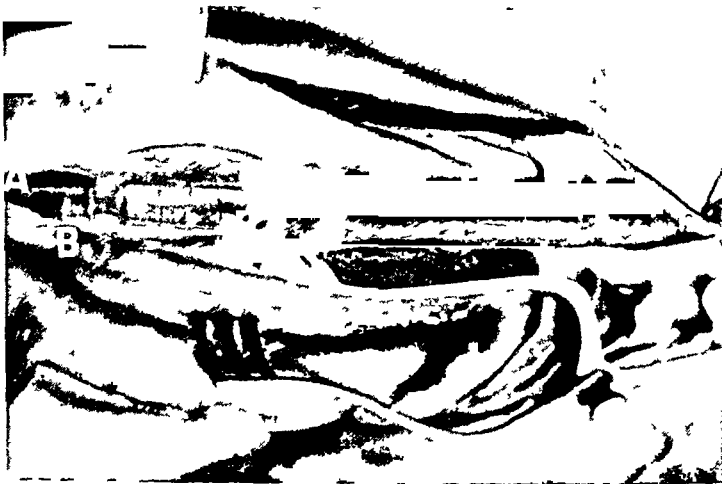


FIG 3—Regional heparinization (A) Showing needle in lumen of artery (B) Proximal to suture line

Venous Grafts—In an earlier report the different methods of administering heparin were described, and suffice it to say here that the term "regional heparinization" has been coined to describe the injection of sufficient heparin into an artery proximal to a suture line (Fig 3) to affect the clotting time locally in that vessel and in the blood returning from that extremity, but not

to change the clotting time of the whole blood stream "General heparinization," on the other hand, is a term employed to denote that the clotting time of the blood in all parts of the body has been increased, and this has been effected by a continuous intravenous injection

To study the effect of regional heparinization, segments of carotid artery varying from one to three and one-half inches in length were excised, and a similar length of external jugular vein, removed from the same animal, was anastomosed at both ends to take the place of the segment of artery removed. The veins stood the pressure satisfactorily and, with regional heparinization, the lumen was kept patent in 70 per cent of 25 such cases (Figs 4, 5, and 6). Further research is in progress on this subject which will be detailed in a subsequent communication



FIG 4—Venous grafts (1) Recovered 48 hours after grafting (2) Recovered eight hours after grafting (3) Recovered eight days after grafting

Peripheral Embolism—Our experience with embolectomy⁶ is now sufficiently great to show that while this operation is useful in trained hands in early cases, it is of no value where the embolus has been lodged for more

FIG 5



FIG 6

FIG 5—Suture line and graft patent three weeks later
FIG 6—Showing change in wall of vein graft after six months

than 12 to 15 hours. In these, the damage to the intima is such that after the removal of the embolus a thrombus quickly occludes the artery again and so spoils the operation. To study this, a series of experiments was per-

formed on dogs in which the femoral and carotid arteries were opened by linear incisions and plugs of sterilized foreign body and blood clot placed at bifurcations. The incisions in the vessels were closed and the plug left in situ for from 24 to 72 hours. The lumina of the vessels were then cleared through an incision at another spot. In nine controls treated in this way, all the vessels rapidly became occluded again by a thrombus. In eight others, after similar treatment and with either regional or general heparinization, thrombosis did not occur and the vessels all remained patent (Fig 7A).

Splenectomy—To investigate the effect of heparin in the portal circulation, in a control group of eight dogs, the spleen was removed and the splenic vein injured by crushing it over a linen suture lying in its lumen. Ten days later the veins were removed and in all the controls these were occluded. In eight other animals, a similar operation was carried out, with similar

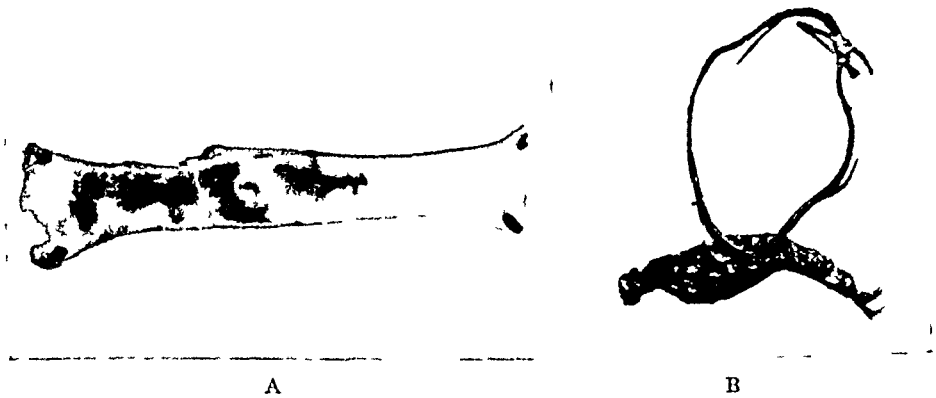


FIG 7—(A) Shows artery three months after embolectomy. Suture lines healed. (B) Shows lumen of splenic vein clear.

injury to the vein, and general heparinization was continued for 72 hours. Seven days following this, the veins were removed and in all the lumen was patent (Fig 7B). While there was satisfactory evidence that heparin would prevent thrombosis in the peripheral circulation, it was not known what effect it would have in the portal circulation. This would appear to be evidence that this substance will prevent thrombosis in the portal system.

Transplantation of Organs—Without very great care in technic, Carrell's transplantation of organs has been carried out and the circulation has been restored and maintained successfully for many months with the aid of heparin. Using our technic, control cases failed when heparin was not used.

Administration of Heparin to Human Beings—With the knowledge that heparin was nontoxic and would prevent thrombosis and clotting in blood vessels in animals, it was decided to carry the experiment further and try it on clinical cases in the wards of the hospital.

Published reports² describe the first efforts at giving heparin to patients in the Toronto General Hospital and contain descriptions of methods of giving it and the effects obtained by the different methods.

To determine if heparin was toxic, it was administered intravenously to

several patients but it was disappointing to find that about half of them showed toxic effects in the form of headache, nausea, vomiting, faintness, pallor, chills, rapid pulse and a fairly marked fall in blood pressure. Its further use had to be abandoned, therefore, until a still purer preparation could be produced. This was finally accomplished by Charles and Scott¹ when the crystalline barium salt was isolated, and since then no toxic effects on patients have been observed. As a result of its intravenous administration, the blood clotting time can be maintained for as long as 40 days at a level three or four times the normal, and it is possible to administer it to the average patient on the wards without the anxiety that formerly attended its use.

Before it could be considered safe to use heparin in the wards, one had to be assured that its administration would not have a cumulative effect, and to have some idea of how long a time would elapse after stopping the injection before the clotting time would return to normal. It was important to know this as there was always the possibility of a hemorrhage occurring during the administration of the drug. This matter was studied in both animals and patients, and it has been shown that when the administration of the drug is stopped it rapidly disappears from the blood. In patients whose clotting time has been raised to 20 minutes, the effect has completely disappeared in an hour and even when the clotting time was raised to an hour and a half there was a return to normal in an hour and 20 minutes. This knowledge was comforting in one patient, who had been heparinized for four weeks because of phlebitis and who developed symptoms of reactivation of an old duodenal ulcer and a hemorrhage. With the discontinuance of the heparin the bleeding ceased and patient recovered.

Negative Phase—Neither in the experimental animals nor in human beings, when the effect of heparin has worn off, has there been any demonstrable change in the blood. The clotting time does not become shorter than the normal time, the sedimentation rate, van den Bergh reaction, prothrombin index, platelet and red and white blood counts do not change. In none of the cases that have received heparin clinically, has there been any evidence of late or residual effects such as recurrent thrombosis or embolism after the clotting time returned to normal.

Arterial Anastomosis and Venous Grafts—Thus far, we have not had an opportunity to employ this operative procedure in the hospital but hope to try it when a suitable patient appears. Not infrequently, surgeons are confronted with a situation where a tumor involves an important artery, and in which the artery must be ligated off to allow removal of the tumor. The choice lies between leaving at least part of the tumor or tying the vessel, and in certain instances, as in the case of the internal carotid, this is accompanied by very grave risks. It is proposed under such conditions to remove a segment of the artery, to reconstruct it with a venous or arterial graft, and then to heparinize the patient. It is hoped also in aneurysms, arteriovenous fistulae, and probably in some other diseases of arteries that, after resecting

the affected area, the main trunks can be reconstructed and the circulation restored

Peripheral Embolism—Our clinical experience with heparin in this disease has not been great, as the number of cases admitted to the surgical wards is small, but in the few we have had, the results have been impressive. In none has amputation been necessary and in several the peripheral pulse

FIG 8



FIG 8—Aorta, iliac and femoral vessels patent, suture line at arrow healed

FIG 9

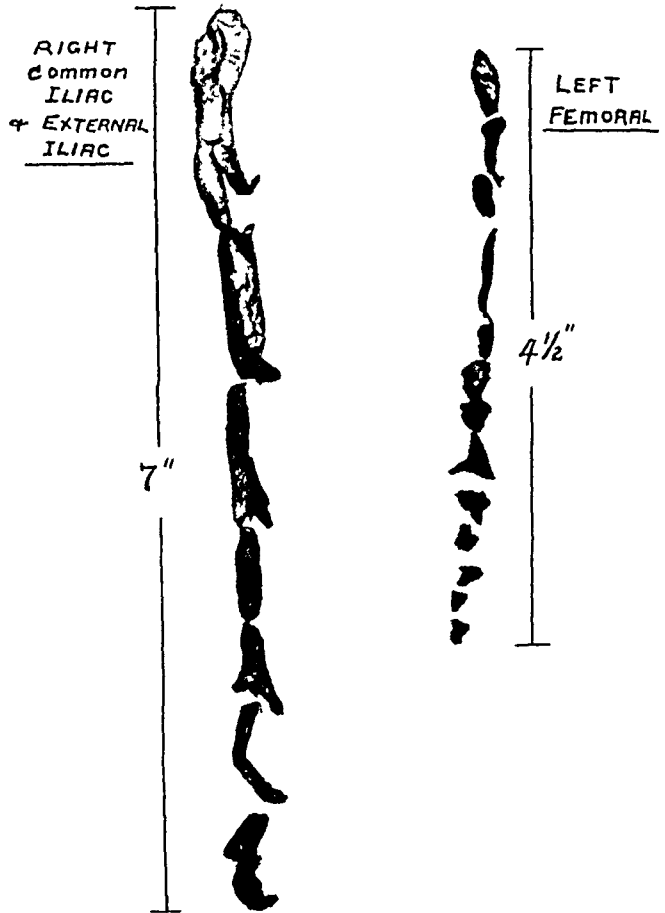


FIG 9—Emboli removed

beyond the occlusion returned and persisted. Such observations, however, are not conclusive, as it is always possible that the recovery occurred through the development of the collateral circulation. However, in one very unfavorable case, a subsequent autopsy enabled us to examine the arteries and to see that a complete restoration of the circulation had taken place. This was a patient who was operated upon 25 hours after the first appearance of symptoms for embolism involving both common iliac and femoral arteries. The emboli were removed but they did not slip out as easily as in earlier cases because of some stickiness of the intima. Before the arterial clamps were removed from the arteries these were filled with a heparin solution. When the clamps were removed, the circulation returned quickly to both feet. From

then on, the patient's blood clotting time was kept above 20 minutes for two weeks, and then the heparin was discontinued. The circulation remained normal and there were no ill effects apart from a moderate sized hematoma in the abdominal incision, which caused no special trouble. However, in the left foot, even though the palpable pulsations in the anterior and posterior tibial arteries remained normal, there was some residual anesthesia and loss of motion. These were nearly complete at first but showed daily improvement, so that at the end of the second week the foot was well on the way to recovery. This was interesting, because of the fact that the circulation was restored and maintained in a leg and foot that had been cut off from nourishment for a sufficient length of time to cause some of the tissues to

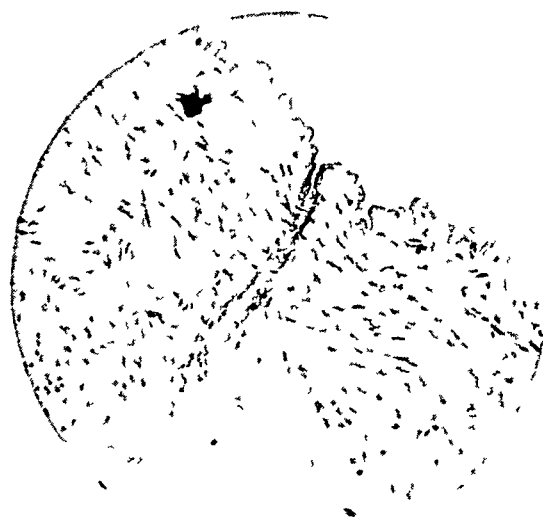
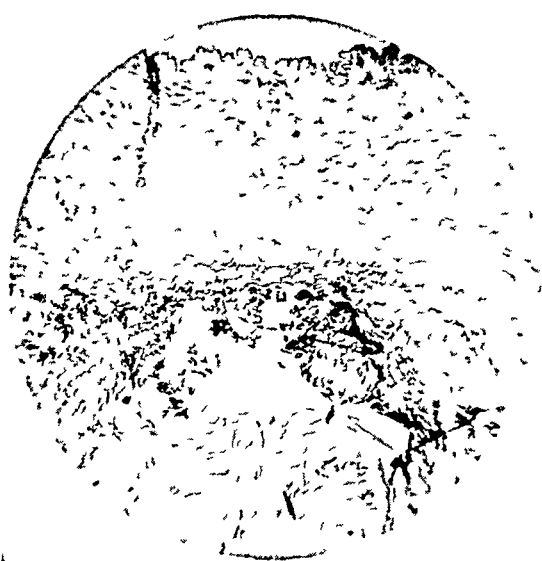


FIG 10—Photomicrograph of the suture line in the wall of iliac vessel (X25)

FIG 11—Photomicrograph showing the intima headed, no thrombosis (X100)

be seriously damaged. On the fifteenth day postoperative, the patient died of other lesions. The aorta, iliac and femoral arteries were recovered (Figs 8 and 9). The vessels were all perfectly clear, with not the slightest sign of thrombosis or blood clot, either on the areas from which the emboli were removed or at the incisions. The latter were healed so perfectly that they could not be found on the intimal surface, except after a very careful search (Figs 10 and 11).

In four other cases of embolism, embolectomy was carried out successfully, and by employing heparin the vessels remained clear, and palpable pulsations in the peripheral arteries were restored and maintained.

This is a field where, from experimental evidence as well as from the results in a few clinical cases, it would appear probable that heparin can be of great assistance. Also, it might be worth while giving heparin in cases of embolism which are seen too late to have the embolus removed, in the hope that heparin will prevent extension of the thrombus and clot, and in this way assist the other measures used in restoring collateral circulation.

Splenectomy—Based on the experimental evidence, five patients in the Toronto General Hospital have been treated with heparin following splenec-

tomy Three were in cases of familial jaundice, which made uneventful recoveries after operation, and are well now, more than one year later In the other two, the spleen was removed to facilitate the operation of complete gastrectomy One case is alive and well, the other died of general peritonitis At autopsy, the systemic and portal vessels were examined and the pathologist reported no generalized thrombosis and fewer and less extensive thrombi than are usual in the stumps of the splenic and other vessels that have been ligated in the operative field While these cases had no complications from thrombosis, it will be necessary to observe the effect of heparin on many more before conclusions can be drawn

Postoperative Pulmonary Embolism—To date, 335 patients at the Toronto General Hospital have been given heparin Except in the first nine cases, the 500 unit per mg preparation has been employed, and with this there have been no toxic effects observed The injection was given in each case in a superficial vein through an ordinary steel needle which stayed at the same spot in the same vein for periods varying from three to eight days without thrombophlebitis developing in a single vein There has been no evidence of phlebitis or thrombosis with embolism developing during, or following, the administration of heparin in any of these cases

In this group, there were 315 cases which received heparin postoperatively These operations included all those performed in general and orthopedic surgery While the incidence of pulmonary embolism is about one in 400 operations, yet, when minor procedures such as transfusion, excisions of cysts and lipomata, *etc*, are eliminated, and some special groups of more major operations are considered, the figures are quite different For example, in the Toronto General Hospital, 2.2 per cent of all operations of partial and complete gastrectomy died of pulmonary embolism, of resection of colon, 3 per cent, of abdominoperineal resection of rectum, 6 per cent, of fractured neck of femur, 4.3 per cent, and of prostatectomy, 7.5 per cent, died of pulmonary embolism

The group of 315 postoperative cases receiving heparin includes many of these types of operation and in none has there been evidence of pulmonary embolism or thrombophlebitis

Pulmonary Embolism—Seven cases of pulmonary embolism with infarcts varying in number from one to six in each case, arising from thrombophlebitis of the legs, were treated with heparin All the cases showed rapid clinical improvement within 24 hours and had less pain in the legs and chest Although several of the cases had recurring embolisms of serious proportions every few days, before the intravenous injection of heparin was started, no further embolisms, with one possible but not proven exception, occurred after the treatment was started

While the group of cases is too small to draw conclusions from, still it offers some hope that this method of treatment may be useful in such cases

Phlebitis—Twenty-eight cases of spontaneous thrombophlebitis, including several cases of phlebitis migrans, have been treated with heparin There

has been no evidence of embolism in any of these and the clinical signs and symptoms, pain, swelling, tenderness and fever, appeared to show more rapid improvement than in a control group

The Time Heparin Is Started in Postoperative Cases—From the experimental² and clinical experience, it has been proven, fairly conclusively, that heparin will not dissolve a blood clot or a thrombus, either in vivo or in vitro. From this evidence, it may be assumed that if the bleeding has been stopped at the time of operation, heparin will not start a hemorrhage. To obtain hemostasis, as in all good surgical technic, all the larger and medium sized vessels should be tied off, or sealed with a cautery, and the small vessels will look after themselves and will not be the source of a hematoma. It is possible, however, that vessels which do not bleed when the patient is in shock may bleed with a rising blood pressure. If such a vessel is bleeding, heparin will certainly allow it to bleed more than it would do otherwise.

For these reasons heparin is not administered for from four to 24 hours following operations, to allow the normal processes which control bleeding to operate. If there is any doubt about oozing or bleeding, the patient is not given heparin.

Hematoma Following Administration of Heparin—With the above mentioned precautions, only four cases developed hematomata postoperatively, while under the influence of heparin. The hemorrhage stopped when heparin was discontinued and all the patients recovered.

Method of Administration—As there are no toxic effects, the patients in the wards have received general heparinization. The ordinary intravenous drip is used, and to the salt solution sufficient heparin is added to increase the clotting time of the patient to about 15 minutes. Usually, heparin is added in the proportion of 10 units of heparin to 1 cc of saline, in the average patient this should run at about 25 to 30 drops per minute. The rate, however, is adjusted, according to the effect on the clotting time, and this is estimated every few hours until the correct rate of injection can be determined. Further details on this aspect of the subject have appeared in a recent publication.³

The Time Heparin Is Discontinued—The time thrombosis begins following operations is purely a matter of conjecture at present, but if stasis, changes in the composition of the blood and eddying play a part, the patient under anesthesia, with a lowered blood pressure, in shock, and in cramped positions on the operating table or in bed, is under ideal conditions for the initiation of the process. The methods of combating these conditions, as described by many writers, do a great deal in decreasing the incidence of embolism, and it is hoped that the remaining difficulties may be overcome by the use of heparin.

The injection is discontinued when the patient has regained normal activity, i. e., when the factors thought to contribute to the production of thrombosis have ceased to act. This time has been reached when shock has passed and the blood pressure and circulation are normal, the incision has healed

and is not painful, so that deep respirations are possible, the patient feels well and energetic and moves about actively in bed and can do exercises, distention is gone, the appetite has returned and the gastro-intestinal and urinary functions have returned to normal, the chest is clear and the temperature and pulse are normal

Selection of Cases—It is hoped that the method of investigation, used by Bancroft and his coworkers,¹ will help in selecting those cases which are most likely to develop thrombosis. It is hoped that in these cases heparin, in appropriate amounts, may prevent the formation of a thrombus and thereby prevent embolism. Before starting treatment, the blood clotting time, prothrombin index, platelet count, bleeding time and the other ordinary blood analyses must be ascertained.

Complications Resulting from Giving Heparin—As there are no toxic effects, and hemorrhage need not occur if the proper precautions are taken, heparin may be given, in appropriate amounts, in any postoperative case. If, however, there is active hemorrhage, heparin should not be given.

Indications for the Use of Heparin—(1) *Postoperative Cases*—A patient, in whom active thrombosis is detected either following an operation, or during an illness, or who has had a pulmonary embolism, is probably in grave danger, and, in the light of our present knowledge, would probably benefit from the administration of heparin. Until the methods of detecting those cases likely to develop thrombosis are perfected, the group of postoperative cases likely to develop this complication should be treated. As this investigation is still in the experimental stage, further indications and limitations may be discovered.

(2) *Phlebitis, Embolism, Operations on Blood Vessels*—While our clinical experiences with the use of heparin are limited in these types of cases, the experimental evidence, especially in operations upon blood vessels, gives very strong support in favor of its value. In suturing of vessels, repair of aneurysms and arteriovenous fistulae, heparin may be of great assistance in obtaining good results.

(3) *Blood Transfusion*—In blood transfusion, heparin can be employed quite satisfactorily instead of citrate. To prevent coagulation, the donor may be heparinized, as Hedenius⁷ has shown, or heparin may be added to the blood as it is removed from the donor. It is useful also in removing blood for the ordinary laboratory tests where citrate or oxalate is commonly used.

(4) *Coronary Thrombosis and Cerebrovascular Thrombosis*—Other possible fields in which heparin might be useful, but which have not been explored, are coronary thrombosis and cerebrovascular thrombosis. While the administration of heparin could not remove the thrombus already present, it might prevent extension of the process. Extension, in both diseases, may be manifested in some cases by recurrent attacks or extension of the lesion within a few hours or days. It might have a useful rôle, also, in lateral and cavernous sinus thrombosis and in progressive thrombosis on heart valves.

CONCLUSIONS

(1) Heparin in its purified form is nontoxic, both experimentally and in human beings

(2) In lesions where intravascular clotting is a problem, heparin may be useful

(3) Experimentally, heparin will prevent thrombosis in blood vessels, clinical results thus far obtained do not contradict this conclusion

(4) As all this work is in the experimental stage, final conclusions cannot as yet be drawn

We wish to take this opportunity to acknowledge the assistance of Mr L B Jaques, Dr T S Perrett, Dr R Wilkinson and Dr R McKenzie. The financial assistance of the Banting Research Foundation in making grants at various times to the assistants is also gratefully acknowledged. The heparin used in the earlier stages of this work was supplied without charge by the Connaught Laboratories.

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DISCUSSION —DR FREDERIC W BANCROFT (New York, N Y) I am impressed with the marvelous work that has been done by Doctor Gallie and his group in the use of heparin as an anticoagulant. There is no doubt that anticoagulants are an adjuvant in the treatment of thrombosis and embolism.

In discussing thrombosis and embolism, the physical factors of trauma, venous stasis, dehydration and infection enter into every case, and the blood clotting factors of the individual are a secondary cause. Therefore, one must focus one's attention upon preventing the physical factors. Nevertheless, it is obvious that some patients are more susceptible to thrombosis and embolism than are others, and it is this type of case that we must guard against. Doctor Homans has very truly said that the prevention of thrombosis and embolism is gunning for the hundredth case. The criticism has been brought against Doctor Stanley-Brown's and my previous reports of our prophylactic therapy for thrombosis and embolism, that we had not given analyses of the types of cases that we have treated that might be susceptible to embolism, so I should like to just briefly review 1,646 consecutive cases which we had studied by means of the plasma clotting index and the fibrinogen test which we presented to this Society a year ago, and which we have treated by the prophylactic regimen we described. We have included in this list the types of cases we felt were susceptible to thrombosis and embolism. As you have

seen by the figures presented by Doctor Gallie's group, these varied from 2 to 6 per cent in the Toronto Hospital series, before they had started the use of heparin

In the analysis of our cases, about 14 per cent showed high blood clotting indices, and all of the accidents reported were in this group. It so happens, however, that the four deaths from embolism were cases in which we had had the blood clotting factors but had not put on prophylactic treatment. In the series that we had placed on prophylactic treatment, no accident occurred. This may sound strange, but where one has continued the study of cases for a number of years, every now and then the analysis of the blood clotting factors will be overlooked in the study of a patient and, therefore, if he has a high clotting index, prophylactic therapy may not be instituted. In one of our cases, for instance, of phlebitis, the patient was a young woman, age 21, who had had an appendectomy and freeing of adhesions about the ascending colon. It was noted on her fifth postoperative day that her clotting factors were high, and this was again noted on the ninth day, but she seemed to be doing so well that she was not given sodium thiosulphate or placed on a diet. On the eleventh postoperative day she developed phlebitis in her left femoral vein.

The following tables I believe are self-explanatory.

PERCENTAGE OF THROMBI AND EMBOLI ACCORDING TO DISEASES†
TESTED CASES*

Fifth Avenue Hospital Series

Diseases	No of Cases	Phlebitis	Per-centage	Emboli	Per-centage
Appendices	398	1 Phlebitis	0.2	1 Embolus, nonfatal 1 Embolus, fatal	0.5
Herniae	199	1 Phlebitis	0.5	1 Embolus, fatal	0.5
Gallbladders	142	1 Phlebitis	0.7	1 Coronary thrombosis, fatal	0.7
Hysterectomies for fibroids	121	1 Phlebitis	0.8	0	
Stomach resections for ulcer or Ca	43	1 Phlebitis	2.0	0	
Adhesions	25	1 Phlebitis	4.0	0	
Perineal plastics	87	1 Phlebitis	1.0	0	
Salpingectomy, oophorectomy	110	0		0	
D & C, for bleeding	102	0		0	
Thyroids	37	0		0	
Breast lesions	29	0		0	
Urologic	86	0		0	
Gastrectomy for Ca of esophagus	15	0		0	
Hemorrhoids	40	0		0	
Fistulae	20	0		0	
Colon and rectum, resections	29	0		0	
Infections	63	0		0	
Miscellaneous					
Fractures	100	0		0	
Varicose veins					
Tumors					
Tuberculosis					
Pelvic peritonitis					

Presbyterian Hospital Series

920 cases tested
12 per cent showed high indices
Only 46 per cent of these received prophylactic treatment
No accidents in treated group
Nine accidents in untreated group
Two of these unrecognized as only fibrinogen was high
Control service had 12 accidents

New York Hospital Series

575 cases tested
13 per cent showed high indices
Only 49 per cent of high were treated
Treated group One treated case had a nonfatal pulmonary infarction on the fourteenth day
Untreated group One fatal embolism One nonfatal embolism
Control service Two emboli

† All accidents occurred in the high index group but had not received prophylactic treatment

* 12 to 14 per cent of tested cases showed high indices

The summary of the above 1,646 cases shows that there were three fatal accidents from embolism and one nonfatal, or approximately 02 per cent. There were six cases of phlebitis, or approximately 04 per cent. The tabulation of the results at the New York Hospital and at the Cornell Clinic shows the results of their treatment, but which we have not analyzed fully, as yet, as to the series of cases.

Our prophylactic regimen on a patient showing high clotting factors is to give intravenously for several days 10 cc. of a 10 per cent solution of sodium thiosulphate, to increase fluids by mouth, and to restrict the fats and carbohydrates in the diet.

On analyzing the results of the work of Doctors Murray and Best with heparin, and ours with sodium thiosulphate, I feel that we are not as far apart as one might believe. It is very possible that sodium thiosulphate has a definite effect in helping the liver liberate heparin, as we know that sulphur compounds can do this. We have of course no proof of this theory.

Diet, we feel, is very definitely a factor. A high protein, high fat diet does increase the percentage of people who are subject to embolus, and a diet low in proteins and fats will diminish the clotting factors, as we have been able to show in both dogs and humans.

Finally, in summarizing the advantages of Doctor Murray's and Doctor Best's treatment, they have been able to perform arterial suture and embolectomy by employing a method that will open up an entirely new field in surgery, and the future will show what a great advance this is. They have also been able to show very much better results than we have in the treatment of thrombosis and embolism after the initiation of the disease. We have been able to abort cases of early phlebitis, but we have had very few good results after it has existed for over 48 hours. Doctor Murray has shown us where they have had cures of phlebitis after it has persisted for a considerable period of time.

The disadvantage, it seems to me, of their procedure is that heparin has a very short duration of action, and, therefore, a continuous intravenous administration has to be kept up from 72 to 120 hours. At present, the average expense per patient amounts to about \$80, which does not entirely

include the discomfort to the patient and the increased nursing cost in giving a continuous intravenous administration over this long period

During the period since 1928 that we have been studying thrombosis and embolism, we have made blood determinations on over 8,000 cases and are convinced that our tests are, in general, an accurate analysis of the clotting tendencies of an individual. We have had only one case of multiple embolism, which was operated upon in another hospital, and which had low clotting factors. With this exception all of the accidents we have examined are in the high blood clotting group. It is true that 12 per cent of post-operative cases show high clotting factors and that only about 1 per cent of the 12 per cent demonstrate an accident. Nevertheless, a large percentage of these cases run a higher elevation of temperature than is normal and may be potential thrombosis or embolism cases.

We believe, therefore, that an analysis of the clotting factors gives us the group in which accidents are apt to occur and that at the present time it is much cheaper to treat these cases prophylactically by sodium thiosulphate than it is with heparin.

We believe that after thrombosis or embolism has occurred, the employment of heparin is far superior to sodium thiosulphate.

It is interesting to note that a number of medical groups have been treating coronary thrombosis by sodium thiosulphate and that the physicians who have been carrying out this procedure feel that their cases have done much better than they did by other methods of treatment. It is too early to place any definite reliance on this procedure. The cases of coronary thrombosis that we have studied have all had high clotting factors.

DR HOWARD LILIENFELD (New York, N. Y.) The only reason that I am discussing this paper is that I asked Doctor Gallie if I might do so. Had I known just what the paper was going to be, I never would have been so forward. I was interested, not so much in heparin, as in the general object which was attained by this group. This is a tremendous advance. Synthetic heparin will be the next step in progress.

I am particularly interested in this question from the standpoint of therapy by means of leeches and then hirudin, which accomplishes the same result. I remember when leeches were used for bloodletting from inflamed regions, to great advantage. But I think the treatment would have done more good, if, after the leech had filled himself full of blood and dropped off, the leech-bite had not been permitted to bleed but had been stopped so as to leave the hirudine in the patient. In all probability the good that the leeches did was to get rid of a certain amount of the local thrombosis which occurred in the infected tissue.

The French have been using leeches for a long time. In the memoirs of the French Academy of Medicine, for March, 1923, there are papers which are of interest. It has been suggested that there was danger of producing embolism from thrombophlebitic veins by using leeches. I do not believe that this is likely to happen.

I have used leeches for a long time, and I have obtained absolutely amazing results. I had two cases of saphenous phlebitis, first one side and then the other, following prostatectomy, the thrombophlebitis extending into the femoral vein. The patient, years ago, had had the same type of infection and had been in bed for nearly six months. This time, he was out of bed three days after I had treated him by means of leeches. Then, about ten days later, the same condition appeared in the other leg, and leeches were again employed with the same result. The man has remained well for the past eight months.

A friend of mine, a doctor in New York, had thrombophlebitis recently in the left leg. I suggested leeches and his doctor said, "Oh, that won't do any good," and he advised continuing only bed rest. I met the doctor at a medical meeting only three or four days ago, looking perfectly well, and I said, "Too bad you didn't use leeches." "Oh," he said, "I did use leeches and I was out of bed and well in two weeks." If he had used heparin, he probably would have recovered just as quickly and, of course, heparin has the advantage over hirudine in that it has now been made available, whereas, hirudine still has not been supplied commercially.

Dr. Arthur Master, not long ago, read a paper on coronary thrombosis in which he showed that this disease is very common—more so than most surgeons are apt to believe—after operations of any kind. I believe that here heparin would be valuable. This was hinted at in today's communication, and I think the treatment ought to be used as a routine.

There is only one other point that I want to make. I was talking with Dr. Carl Koller, the discoverer of the anesthetic value of cocaine, and I mentioned this action of leeches, not at the time knowing about heparin. "Oh," he said, "that's fine, I'm going to use it in the next case of central retinal embolism that I get." I believe that if it is used immediately, it may save the sight of the eye.

Of course, heparin is not yet generally obtainable, but it soon will be. In the meantime, I certainly would recommend, in any case of angina where the disease is supposed to be due to thrombosis, that leeches should be applied. You can use as many as ten or 15. They do not need to be put on near the heart.

DR. MONT R. REID (Cincinnati, Ohio). I rise only to confirm the great value in the use of heparin in experimental work and also to answer the question I know must have occurred to Doctors Gallie and Murray as to how one could keep our experimental arteriovenous fistulae open and make any worthwhile studies.

The observations we made upon fistulae between the aorta and vena cava would have been absolutely impossible without the use of heparin. As it was, we could prevent any clotting at all in that type of fistulae for four or five hours, or longer, if we had wanted to continue the experiments.

A STUDY OF EXPERIMENTAL AND CLINICAL SHOCK WITH SPECIAL REFERENCE TO ITS TREATMENT BY THE INTRAVENOUS INJECTION OF PRESERVED PLASMA

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THE term traumatic shock is ordinarily used to indicate the state of circulatory collapse which follows injury, and is characterized by an actual decrease in the circulating blood volume.^{1 2} The mechanism of this reduction in blood volume is not entirely understood but is, for the most part, the result of obvious and concealed bleeding at the site of injury plus an excessive loss of blood plasma in the traumatized tissue.^{5a b} Thus traumatic shock differs from the shock due to acute hemorrhage where the fluid loss is mainly whole blood, and from that associated with burns or intestinal manipulation where it is essentially blood plasma depletion. The treatment of these three types is based on the restoration of the depleted blood volume, but the problem presented by a patient who has had an acute hemorrhage is vastly different from one with extensive contused wounds or following severe burns. One reason for this difference is found in the excessive loss of plasma which traumatic shock and that due to burns have in common.

Following an acute hemorrhage, the blood volume is diminished by an actual loss of whole blood and the patient will show the typical signs of circulatory collapse. If the bleeding is controlled before the amount of blood loss is too great, the body will tend to build up the depleted volume by drawing fluid from the tissue spaces into the circulation. This process tends to increase the blood volume and with the intravenous injection of saline, the volume can be restored to within normal limits. If the same picture of collapse results several hours following a contused wound, the problem becomes more complicated. There is the same reduction of the blood volume, but there has also been a greater loss of plasma than of the cellular elements from the blood stream.^{5a b} This loss of plasma is thought to be due to an increase in the permeability of the small peripheral vessels. The addition of saline in this instance will dilute the remaining protein and thus lower its osmotic pressure. This reduction of the osmotic pressure will result in further fluid loss from the blood stream and consequently the saline is of only temporary value. The treatment of this condition demands the addition of protein to increase the colloid osmotic pressure of the blood.

The transfusion of whole blood has been found to be the most satisfactory method of restoring the plasma proteins, the blood volume and in the

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case of hemorrhage, the depleted cells. However, there are two tangible disadvantages in the use of whole blood. This first is its availability. Donors may not be readily available when necessary for emergency use and the preparations for transfusion are, at best, time consuming. These difficulties have been partially overcome by the use of blood banks and donor bureaus. However, whole blood can be preserved for only a limited time and the dangers of transfusion reactions from preserved blood which has hemolyzed are always present. The second disadvantage is best exemplified in shock due to burns when there is excessive loss of plasma and concentration of the blood. In this case, the addition of whole blood adds to the already increased viscosity by increasing the volume of red cells.

The use of blood plasma would overcome these disadvantages in certain cases. A method of preserving plasma for extended periods of time has been described by Flosdorf and Mudd⁴. Their method depends on the rapid dehydration of the serum or plasma in the frozen state under a high vacuum. In this manner, the material can be dried and preserved, and when rediluted, retains its original biologic and chemical characteristics. This procedure would make possible the preservation of large amounts of plasma for use in the emergency treatment of shock. Theoretically, it is of most value in those types not associated with gross hemorrhage, but its efficacy can only be determined by experimental and clinical use.

The importance of the loss of plasma in experimental shock has been demonstrated by Blalock⁷. He has shown that dogs do not tolerate the loss of plasma as well as the loss of proportionate amounts of whole blood, and that with hemorrhage into tissues following trauma, there is a continued loss of plasma after the acute bleeding subsides. There is also experimental evidence supporting the use of plasma in the treatment of shock. Mann⁸ and Harkins⁹ have shown that the intravenous use of serum and plasma is an efficient method of treating experimental shock in which hemorrhage is not a major factor. The injection of plasma in treating the shock due to burns restores the protein which has been lost and does not increase the viscosity of the blood. Colloidal solutions of gelatin and gum acacia have been used as substitutes for plasma to increase the colloid osmotic pressure of the blood⁸. Gum acacia has been used most frequently, and Erlanger and Gasser^{10a, b} have demonstrated its value in experimental shock. The clinical use of acacia has been attended by some untoward reactions,¹¹ but it is probably the most satisfactory substitute for whole blood or plasma.

In order to determine the advisability of using dried plasma in the treatment of shock, two factors must be investigated. First, does the lyophilic process change the characteristics of the plasma? Bond and Wright¹² have demonstrated that it is not changed and have also shown that the preserved plasma is of value in treating experimental hemorrhage. Second, in what types of shock will the plasma be most efficient? During the past year the following experiments have been devised in our laboratory to test its effectiveness in experimental shock with and without hemorrhage, and to com-

pare the dried plasma with the other commonly used intravenous fluids. The first method was to cool the peritoneal surface of dogs. In this manner the typical syndrome of shock can be reproduced without any significant hemorrhage. The second method was traumatization of an extremity similar to that used by many investigators^{1, 4, 10}. The shock produced by this method is associated with considerable hemorrhage into the extremities. The changes in the plasma proteins and the blood volume were considered of prime importance in evaluating the type of shock produced.

A large amount of experimental work has been done in an effort to determine the physiologic mechanism involved in the blood volume reduction of shock. A few of the outstanding contributions will be reviewed but no attempt made to summarize the entire literature on the subject. The theory of traumatic toxemia was expounded by Cannon in his monograph entitled *Traumatic Shock*¹. This, in brief, is that a histamine-like toxin is elaborated from traumatized tissue which produces dilatation and an increase in the permeability of capillary walls. This permits transudation of plasma from the blood stream with the resulting diminution in the total blood volume. Cannon produced shock by traumatizing the extremities of animals, but was unable to account for the decrease in total blood volume by the local loss of fluid at the site of injury. His theory was the accepted concept of shock until Blalock⁷ and Phemister¹¹ were able to account for the decrease in blood volume by local fluid losses in traumatized extremities. They recognized that the extravasated fluid extended along fascial planes into the groin and retroperitoneal tissues. In their experiments, they weighed the entire lower quarters of the animals and could thus account for the entire fluid loss on the traumatized side. They were unable to demonstrate a circulating toxic agent in the blood stream following trauma, so could not support Cannon's theory.

The rôle of the sympathetic nervous system in shock is important. In 1917, Guthrie¹⁴ had noted that section of the nerves to the leg of a normal animal produced an increase in the blood flow from the extremity of 22 per cent, in a shocked animal, an increase of 76 per cent. Erlanger and Gasser^{10e, d} noted marked vasoconstriction resulting from intestinal manipulation. They also produced shock in dogs by repeated injections of adrenalin. Rapport¹⁵ has also found hyperactivity of adrenal function in experimental shock. Freeman^{16, 17} has demonstrated that prolonged overactivity of the sympathetic nervous system can, in itself, produce a diminution in the blood volume. Recent work by O'Shaughnessy and Slome¹⁸ tends to indict a combination of these last two factors as the underlying principle of traumatic shock. They suggest that the diminution in blood volume is due to an additive effect of local fluid loss plus sympathetic overactivity. The latter factor is pictured by Harrison¹⁹ as an intense generalized arteriolar spasm and anoxemia, which result in damage to the capillary walls causing an increase in their permeability and loss of plasma from the circulatory bed.

Many investigators have shown that the plasma proteins become con-

centrated as the state of shock progresses, but little attention has been given to the albumin and globulin fractions of the plasma. Erlanger and Gasser^{10e} have produced shock by manipulating the intestines and found that fluid was lost through the serous surfaces. This fluid had the same albumin globulin ratio as the blood plasma. The fluid lost in the vesicles of burns corresponds in protein content to the plasma, but the ratio of its fractions has not, to our knowledge, been investigated. In the type of shock produced by peritoneal cooling there is a characteristic alteration of the albumin globulin ratio, which adds further proof that at least a part of the depleted blood volume is due to an increased permeability of the capillaries.

METHODS—The general plan of the animal experiments was to study the shock produced in dogs and to determine the therapeutic effect of saline, gum acacia, whole blood and dissolved processed plasma when administered intravenously. The solutions were injected after the blood pressure had been maintained at a level of 70 Mm. of mercury for one hour. The volume of fluid injected in each experiment corresponded to 10 to 15 per cent of the normal blood volume. The acacia was prepared in a 15 per cent solution and the preserved plasma was dissolved to its original volume in saline just prior to the injection. The blood pressure and the general condition of the dogs were the criteria used in evaluating the response of each dog to the treatment. In the clinical study preserved plasma is substituted for whole blood in transfusing patients exhibiting definite signs of shock, resulting from trauma or from burns. The amount of plasma injected is equal to the protein content of a 500 cc. transfusion and is dissolved in saline to its original volume. In both animal and clinical use the plasma is obtained from citrated blood by centrifugalization.

The processed plasma was prepared by the lyophile method of Flosdorf and Mudd,⁴ which depends on the rapid dehydration of the frozen plasma in a high vacuum. The apparatus was constructed in our laboratory according to the plan outlined by them but was modified in minor details to meet our requirements (Fig. 1). The plasma was processed and preserved in one liter pyrex flasks which have a sufficient inside surface area to safely dry 300 cc. in each container. The vacuum was maintained in the bottles after the process was completed by compression of the rubber tubing with a beveled brass ring (Fig. 2). The freezing pans were so constructed that the vacuum could be developed while the containers were still in the freezing mixture. This was found to be of definite advantage when processing large volumes because it prevented thawing before the operating equilibrium of temperature and evaporation had been established. The human plasma for clinical use was prepared under sterile precautions and passed through a Berkefeld filter immediately before processing.

Two methods of producing experimental shock were used. (1) Cooling the peritoneal surfaces, and (2) trauma to an extremity. Healthy dogs were used in all experiments. In the first method the abdominal cavity was exposed under aseptic precautions and the peritoneal surfaces cooled by placing

cold saline packs between the folds of the mesentery. These were replaced as they became warmed and the procedure continued for one to one and one-half hours, depending on the size of the dog. The abdomen was then closed. At 15 minute intervals, blood pressure readings were taken by direct needle puncture of a femoral artery. The second method of inducing shock was traumatization of a posterior extremity as described by Blalock.⁵

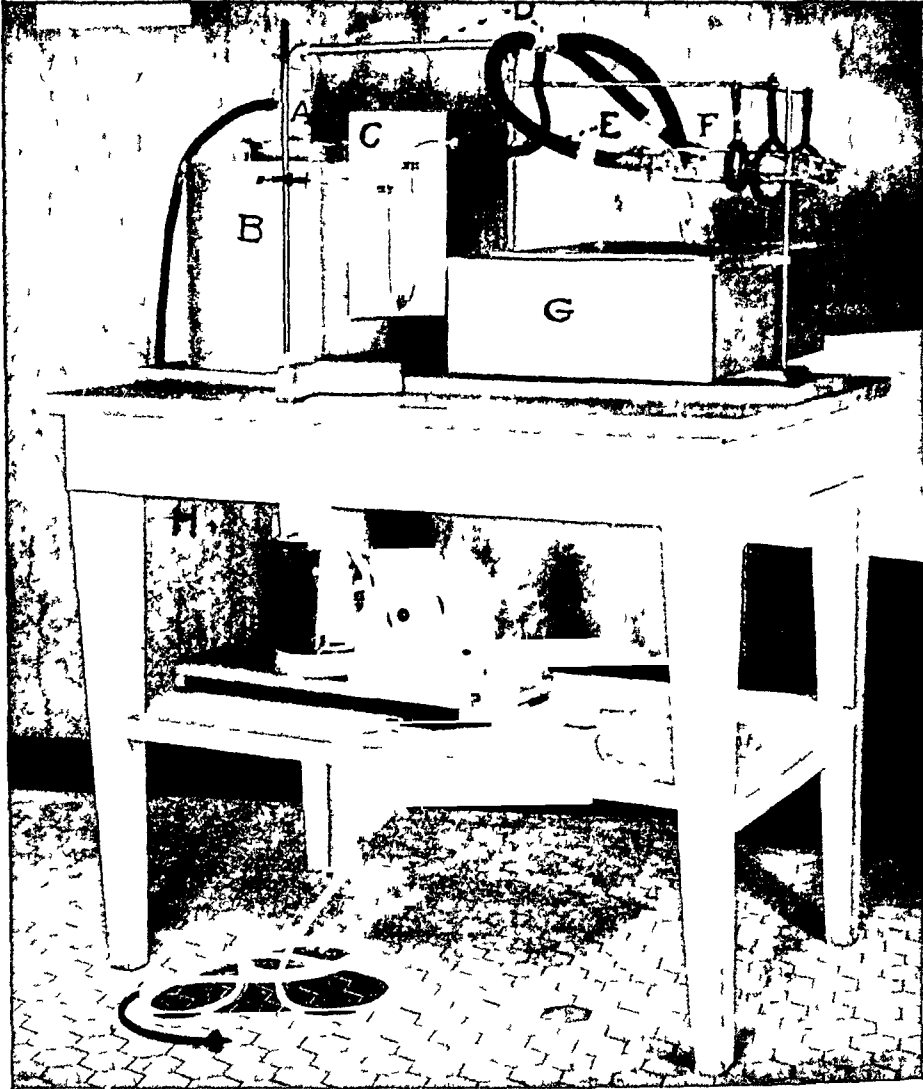


FIG 1.—The modified "Lyophile" apparatus for preserving blood plasma. (A) Condenser (B) Insulated container for dry ice (C) Vacuum gauge (D) Three way manifold (E) Rubber pressure tubing (F) Pyrex containers (G) Freezing pans (H) Vacuum pump

In these experiments, continuous blood pressure readings were taken by means of a mercury manometer attached to a cannula in the carotid artery. The dogs were anesthetized by the intravenous administration of nembutal (0.32 Gm per Kg body weight), which gives satisfactory anesthesia for three to five hours. No untoward reactions to this anesthetic were noted in these experiments. The pulse, blood pressure and respirations remained well within normal limits when no shocking procedure was carried out.

Blood samples were removed from a femoral or jugular vein using extreme care to avoid venastasis, and the blood was collected into 12 cc graduated centrifuge tubes containing 2 cc of 16 per cent sodium oxalate solution. The blood was centrifuged at 3,000 r p m for 35 minutes, and the hematocrits read directly, deducting 0.5 cc for the volume of white cells. The plasma volume was determined by the brilliant vital red dye method of Hooper, Belt, Smith and Whipple²⁰. The total protein was determined by the macrokjeldahl method as described by Peters and Van Slyke,²¹ using 1 cc aliquots and collecting the ammonia in saturated boric acid solution. The albumin was precipitated by the method of Campbell and Hanna,²² using 21 per cent sodium sulphite solution at 100m temperature and the nitrogen determined by the macrokjeldahl procedure. All samples were checked in duplicate and repeated if the error was greater than one part in 60. The total circulating protein, albumin and globulin figures are the product of their respective concentrations and the total plasma volume. The circulation time was determined by the NaCn method of Robb and Weiss.²³

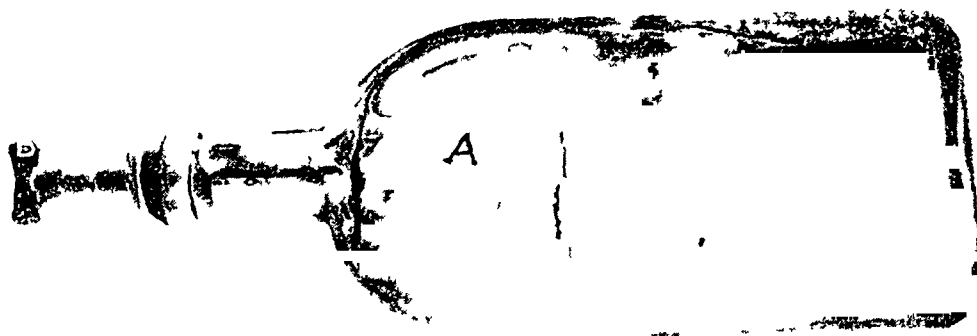


FIG 2—The pyrex bottle containing preserved plasma and sealed with the beveled brass ring (A) Preserved plasma (B) Compressed brass ring

The above blood studies were done routinely on the dogs for several successive days prior to the experiments to establish the average normal values of each dog. The blood values in shock were determined after the blood pressure had been at a level of 70 Mm of mercury for at least one-half hour. It was considered advisable to determine the therapeutic response to the solutions at a level of shock which did not preclude survival of the animal. In this way, the effect of administration of each solution could be tested on the same dog, whose control response was known, and a better comparison of the therapeutic action was possible. At a blood pressure level of 70 Mm of mercury, the process is usually reversible in shock produced by peritoneal cooling, but is irreversible in that produced by trauma to an extremity, and such animals usually die. For this reason the blood pressure was maintained at 70 Mm of mercury for one hour before injecting the solutions. The degree of shock was finally determined by blood volume studies as well as by the level of the blood pressure. This combination affords the most reliable criterion of the depth of shock.

OBSERVATIONS

SHOCK PRODUCED BY PERITONEAL COOLING—The response of the dogs to cooling the peritoneum was quite constant, and with a little experience, the degree of shock produced could be controlled by varying the duration and intensity of the cooling. The pulse pressure declined (Fig 3) and the pulse rate increased shortly after the cooling was begun, but the blood pressure did not decline for one-half hour. The abdomen was closed at the end of one to one and one-half hours, and with no further interference, the blood pressure continued to fall. This decline continued for three to four hours, when the lowest point was usually reached, and the pressure then remained quite constant at a level of 60 to 70 Mm of mercury for eight to ten hours. At this level of blood pressure the pulse was rapid, thready and irregular, the pulse pressure was greatly reduced, and the peripheral veins collapsed. The circulation time was 20 seconds compared with the average normal of ten seconds. The extremities were cool, the rectal temperature was two degrees to three degrees below normal and the mucous



FIG 3—Dog No 676 Pulse pressure in shock.
 Before trauma Half hour after trauma
 B P normal B P still normal
 Pulse pressure 12 Mm Hg Pulse pressure 4 Mm Hg

membranes very pale. If the dogs survived they reacted very slowly from the anesthesia and the blood pressure gradually returned to normal within the next 24 hours. During this period, the animal was apathetic, semicomatose and frequently nauseated. The normal state of animals was not regained for several days. However, after this period, no deleterious effects of the shocking procedure were evident.

The gross changes in the appearance of the peritoneal surface were quite constant. The veins of the mesentery were at first moderately engorged, and with the development of deep shock, became reduced in caliber. Small petechiae developed in the mesentery but did not appear to constitute a significant amount of blood loss. The small bowel was very contracted and peristalsis was quite active. The spleen did not show any gross change. At autopsy, the lungs were not edematous and no edema was noted in the extremities. There was no free blood noted in the intestinal lumen, the mucosa was only moderately congested, and there was no excess peritoneal fluid.

The results of the blood studies on six dogs are recorded in Table I

TABLE I

SHOCK PRODUCED BY PERITONEAL COOLING

A Comparison of the Normal Blood Values with the Values in Shock for a Series of Six Dogs

	Blood Volume		Blood Protein Concentration				Total Circulating Protein		Total Circulating Albumin		Total Circulating Globulin		Red Cell Hematocrit %
	Total cc	Plasma cc	Total %	Albumin %	Globulin %		Gm		Gm		Gm		
Dog No 672 Wt 13 Kg													
Normal	995	485	6 06	4 53	1 53		29 4		22 0		7 4		44 2
Shock B P 70 Mm Hg	715	367	6 67	4 67	2 00		24 4		17 0		7 4		48 6
Dog No 676 Wt 10 7 Kg													
Normal	1,086	543	6 82	4 46	2 36		37 0		24 2		12 8		50 0
Shock B P 70 Mm Hg	740	342	7 82	4 62	3 20		26 7		15 8		10 9		54 0
Dog No 679 Wt 22 Kg													
Normal	2,080	1,000	5 50	4 20	1 30		55 0		42 0		13 0		51 0
Shock B P 70 Mm Hg	1,500	617	6 17	4 37	1 70		38 0		27 0		11 0		59 0
Dog No 682 Wt 17 Kg													
Normal	1,285	753	5 90	3 40	2 50		44 4		25 6		18 8		43 2
Shock B P 70 Mm Hg	970	510	6 36	3 36	3 00		32 4		17 2		15 2		47 0
Dog No 690 Wt 15 Kg													
Normal	1,570	675	5 00	3 95	1 05		33 8		26 6		7 2		54 7
Shock B P 70 Mm Hg	855	398	5 81	4 22	1 59		23 2		16 8		6 4		57 3
Dog No 741 Wt 7 Kg													
Normal	752	440	5 78	4 13	1 65		25 4		18 2		7 2		41 5
Shock B P 70 Mm Hg	565	295	6 66	4 62	2 04		19 6		13 6		6 0		48 0

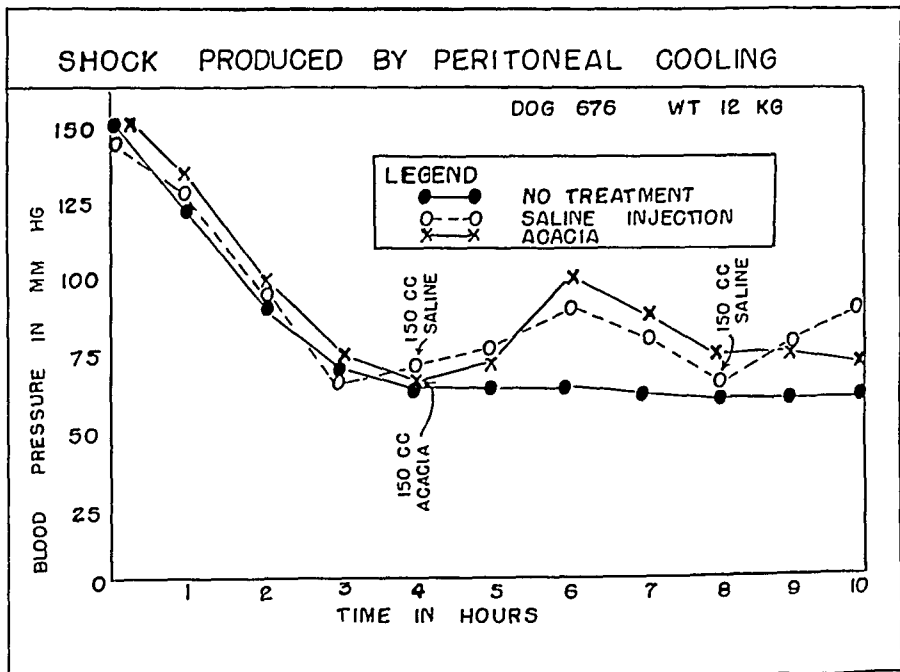
TABLE II

SHOCK PRODUCED BY TRAUMA TO AN EXTREMITY

The Changes in Blood Values Following Trauma

	Blood Volume		Blood Protein Concentration				Total Circulating Protein		Total Circulating Albumin		Total Circulating Globulin		Red Cell Hematocrit %
	Total cc	Plasma cc	Total %	Albumin %	Globulin %		Gm		Gm		Gm		
Dog No 728 Wt 21 Kg													
Normal	2,130	1,380											
One Hour			6 16	3 34	2 82		85				43 4		
Two Hours			6 70	3 51	3 19						42 8		
Three Hours			6 86	3 52	3 34						47 0		
Four Hours			5 94	2 98	2 96						35 2		
	1,380	916	6 22	3 22	3 00		57				34 1		

These dogs were subjected to the shocking procedure a total of 42 times, and the results in each dog were comparable. There was a uniform decrease in the blood and plasma volumes in all of the experiments. The total blood volume was decreased approximately 25 per cent below the normal volume, but there was a greater loss of plasma than of red cells and the hematocrit was increased. The amount of plasma lost was equal to 15 per cent, and the red cells 10 per cent of the normal blood volume. The concentration of the circulating plasma protein was uniformly increased and the change in the albumin-globulin relation was very definite. In every instance the concentration of the globulin in shock was increased in a greater proportion than the concentration of the albumin. The reason for this be-



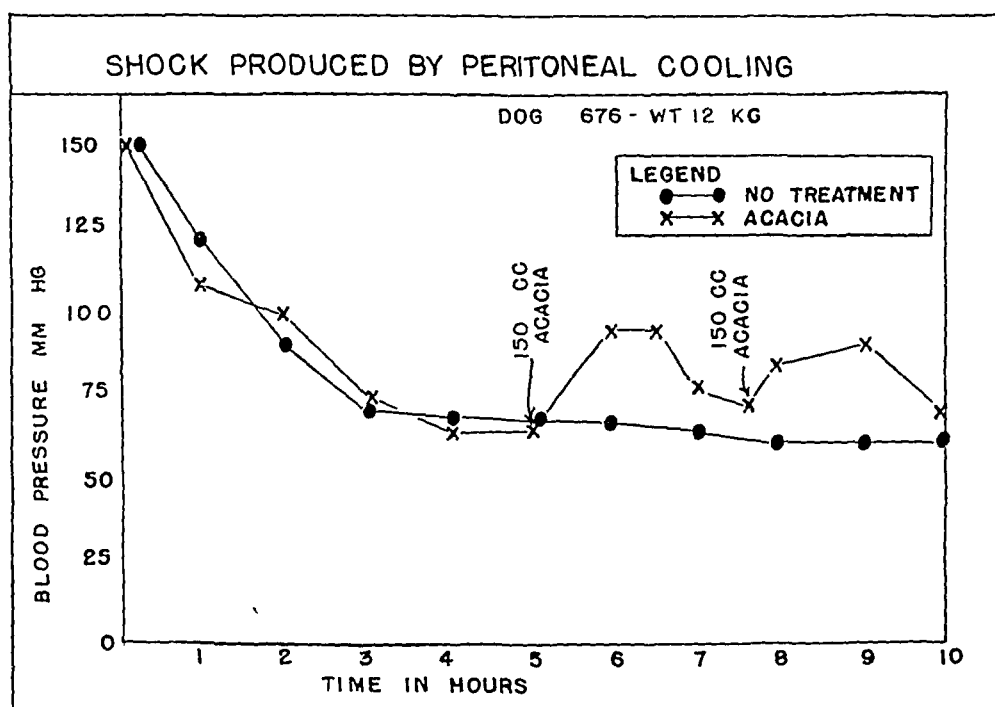
GRAPH 1—A comparison of the blood pressure response without treatment and with the injection of saline and gum acacia (15 per cent solution)

comes evident when the total amounts of albumin and globulin, which constitute the total protein, are calculated separately. Although there was an increased concentration of protein, the total circulating amount was markedly reduced as a result of the decreased plasma volume. The albumin constituted the major portion of this total protein loss while the total circulating globulin was only slightly affected. In fact the loss of albumin averaged more than five times the loss of globulin. This accounts for the increased concentration of the globulin.

The solutions used in treating this type of shock were saline, gum acacia, whole blood and preserved plasma. Each of these solutions was tested on each of the dogs listed in Table I, and in most instances, check experiments were performed on each dog (42 experiments). The blood pressure responses of dogs No. 676 and No. 672 are recorded for each therapeutic agent as they are typical of the results obtained with this series of dogs.

Saline and Acacia—The response to saline and to gum acacia is shown by Graph I. The rise in blood pressure was temporary with both solutions and the ultimate course of the shocked animal was not influenced by the injections. There was no improvement in the pulse rate and no lasting evidence of circulatory stabilization. Acacia had a slightly more beneficial effect than saline because the dogs reacted from the anesthesia sooner and there was an earlier rise in the rectal temperature. All the dogs ultimately survived but showed anorexia and apathy for several days. Graph II indicates that repeated injections of acacia did not alter the ultimate course of this type of shock.

Whole Blood—(Graphs III and IV) The blood pressure response to the injection of whole blood was more lasting than with either saline or

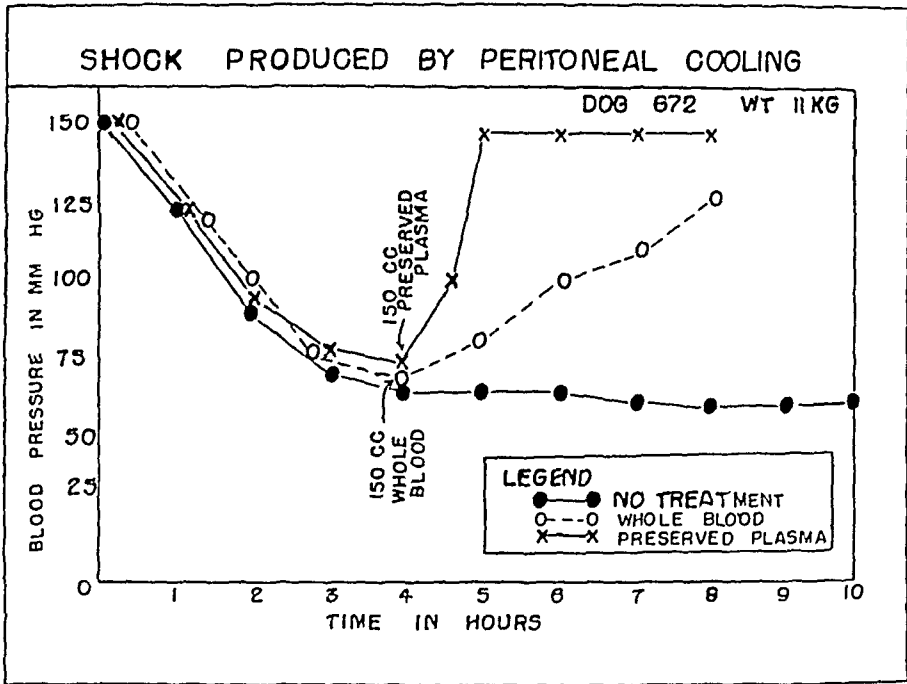


GRAPH 2—The blood pressure response to repeated injections of acacia

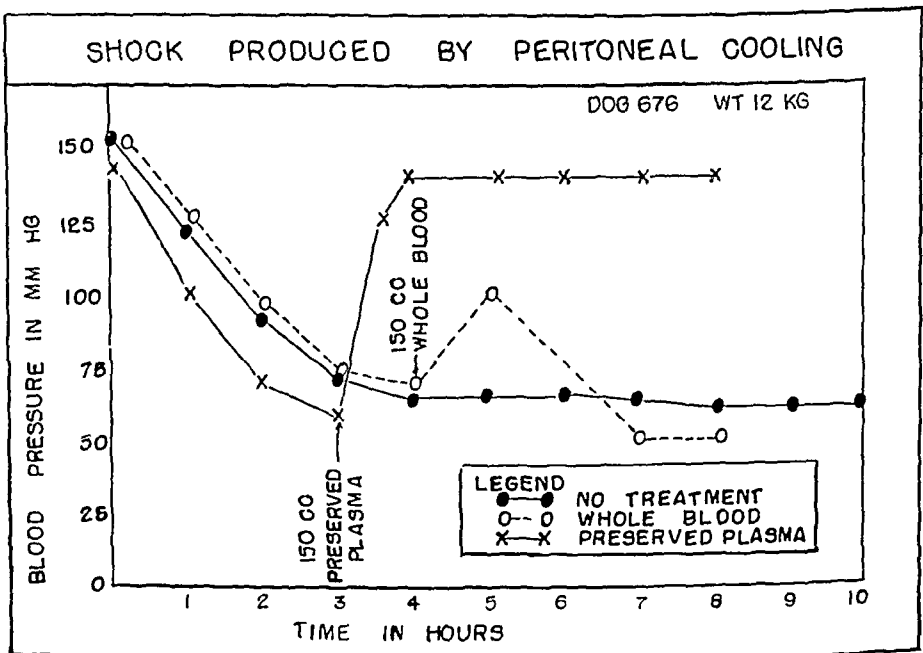
acacia. In all the experiments except one, there was a gradual return of the blood pressure to normal and the animals soon regained consciousness. The pulse became regular, the peripheral veins filled with blood and all the signs of shock subsided. Only dog No 676 showed a temporary response to whole blood, but the blood volume determination in this dog indicated that the degree of shock was more profound than in the other experiments, i.e., a 35 per cent decrease of the blood volume.

Preserved Plasma—(Graphs III and IV) The ultimate result of injecting dissolved, processed plasma was the same as with the injection of whole blood, but the elevation in blood pressure was more prompt and the improvement in the general condition of the dog was more striking. The blood pressure returned to normal within one-half hour after the injection of the plasma and remained stabilized. The dogs regained consciousness, the body temperature returned to normal and the mucous membranes

regained then normal color within one hour. The only exception to this was in an experiment on dog No 676. In this case the blood pressure was falling rapidly and the degree of shock was very profound, as indicated by



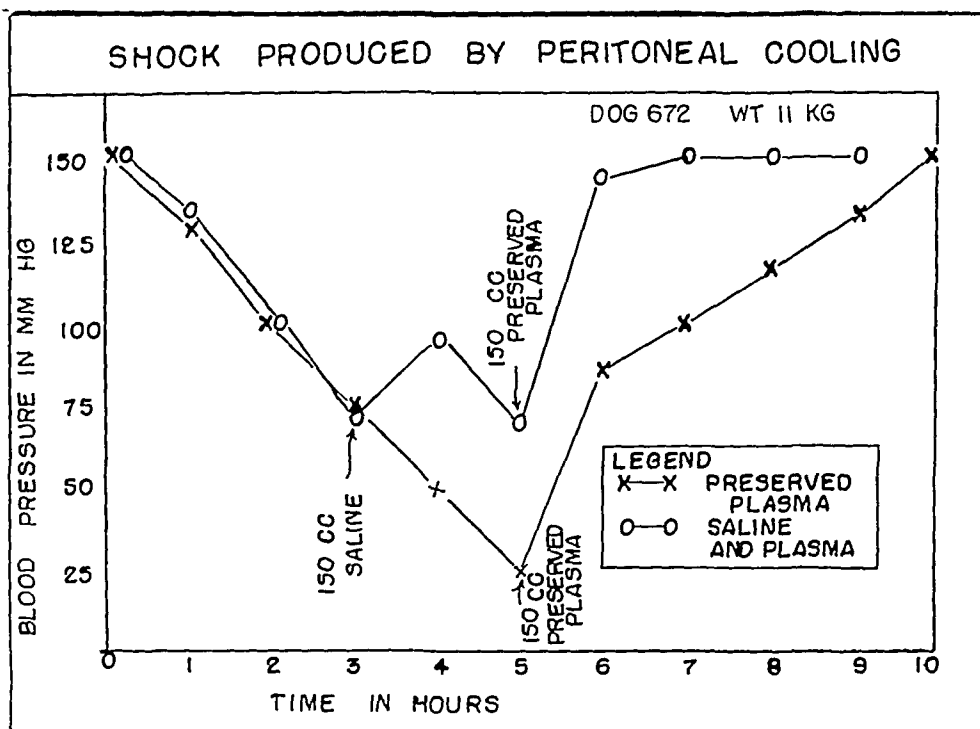
GRAPH 3—A comparison of the blood pressure response without treatment and with the injection of whole blood and preserved plasma



GRAPH 4—A comparison of the blood pressure response without treatment and with the injection of whole blood and preserved plasma

the extremely low blood volume. The blood pressure response in this experiment was not as prompt but the animal survived. The effects of repeated injections of saline and of processed plasma following the saline are con-

trasted in Graph V The processed plasma caused a rapid return to normal, whereas a second injection of saline had only a temporary effect on the blood pressure There was no evidence noted of any untoward reaction to the processed plasma and all of the animals received repeated injections



GRAPH 5—The blood pressure response to preserved plasma in very profound shock and a comparison of saline and preserved plasma in the same experiment

TABLE III

BLOOD VOLUME IN TRAUMATIC SHOCK

The Decrease in Blood Volume Which Occurs Prior to the Decrease in Blood Pressure

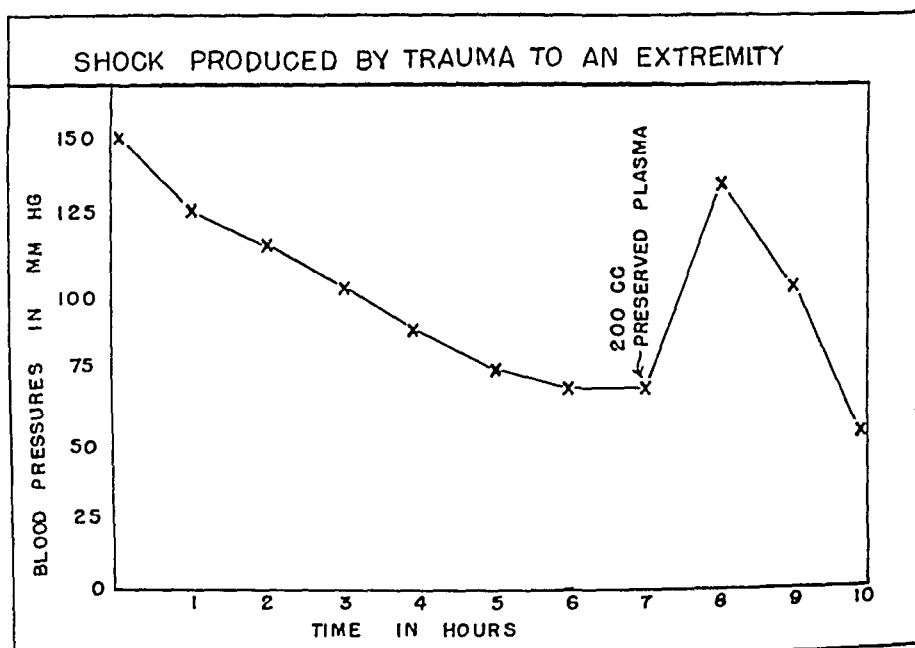
	Blood Volume cc	Plasma Volume cc
Normal	1890	765
One hour following trauma, blood pressure still normal	1400	555

TRAUMA TO AN EXTREMITY —(Table II, Graph VI) The type of shock produced by this method differed in several respects from that produced by cooling the peritoneal cavity The proportion of red cells and plasma lost from the circulation was about equal, which indicated that trauma to an extremity was more nearly comparable to the effects of hemorrhage The plasma proteins and hematocrit were not concentrated The total circulating albumin and globulin were decreased in amounts equal to their normal proportion in the circulating plasma This observation is in striking contrast to that in shock resulting from cooling the peritoneum where the protein loss was preponderantly albumin The blood pressure response to the injection of processed plasma was only temporary In one experiment the

dog survived, but with all others the blood pressure increased temporarily and then steadily declined until exitus occurred

In both types of experimental shock the blood volume began to decline before there was any change in the arterial blood pressure (Table III). The animals showed all the signs of impending shock, such as the increased pulse rate and decreased pulse pressure, but the blood pressure was still normal. However, when the blood pressure did begin to decrease, there was a steady decline until the animal was in profound shock.

Clinical Observations—The dissolved, processed plasma has been utilized in treating patients who were in profound shock resulting from burns and



GRAPH 6—The blood pressure response to the injection of preserved plasma

from trauma. The number of cases are thus far limited, but the results have been decidedly encouraging, especially with burns. The clinical study will be the subject of a future publication.

DISCUSSION—The evidence indicates that whole blood and plasma are superior to either saline or acacia in treating experimental shock and this is in accord with the observations of other authors. In shock produced by cooling the peritoneum, blood plasma is more efficient than whole blood in restoring the normal circulatory conditions. The only obvious explanation for this greater efficiency lies in the excessive loss of plasma in this type of shock. The plasma injections restore the protein which has been lost from the blood stream in a readily available form. Theoretically the injection of albumin alone would be of greater value, but this is at present impossible.

The type of shock encountered in patients cannot be completely reproduced in experimental animals, and it is hazardous to draw clinical impressions from experimental evidence. However, there are certain types

of clinical shock which seem quite similar to the shock produced in dogs by cooling the peritoneum. The shock produced as a result of extensive burns is due largely to plasma loss into the burned areas and plasma injections should be most efficacious in this condition. Also the shock produced in operations in the peritoneal cavity, where there has been very little blood loss, is probably comparable to this condition. There is frequently profound shock associated with gun-shot wounds of the abdomen in which there has been intestinal perforation but very minor hemorrhage. These last two conditions will probably be favorably effected by the injection of plasma.

One of the greatest advantages of the preserved plasma is its immediate availability for emergency use. The effect of plasma on shock resulting from trauma and hemorrhage is transitory, but in spite of this it may well have a definite place in the treatment of these conditions. If the plasma can be used to maintain the blood pressure until the whole blood is available, it will be of unquestionable value. The use of saline in profound shock is generally considered dangerous as it may tend to wash protein out of the blood stream into the tissue spaces. The use of plasma will prevent this danger.

The mechanism underlying the reduction of the blood volume resulting from cooling the peritoneum, invites speculation and the excessive loss of albumin from the blood offers a plausible explanation. The albumin molecule is smaller than the globulin and the average amount of albumin lost is five times greater than that of globulin. The greater proportionate loss of the smaller molecules indicates that there is an increased permeability of the capillaries. This is probably a local process confined to the peritoneal cavity where the capillaries are not accustomed to gross changes in temperature. The effect of the exposure to cold is to damage the capillary walls and thus increase their permeability. This process is not comparable to that in shock resulting from trauma to an extremity, because in this type the albumin and globulin are lost in the same proportion as their concentration in the blood.

The latent period between the beginning decline in the blood volume and the fall in arterial pressure warrants emphasis. The blood pressure will be maintained by vasoconstriction even after a considerable fall in blood volume, but will fall rapidly when the vasomotor system is no longer able to compensate for the depleted volume. This explains the picture of the patient who is still in apparently good condition several hours following injury but rapidly develops circulatory collapse. The early decline in pulse pressure should be stressed clinically in recognizing impending shock.

We do not feel justified in drawing any conclusions from our limited clinical experience. However, the preserved plasma has been used with apparently satisfactory results in shock resulting from burns and from trauma. Its ultimate value can be determined only by extensive clinical application. The hemagglutinins are preserved in the processed product and, at present, it is considered advisable to use only compatible types. The dissolved plasma should always be cross-matched with the recipient's cells, preferably by

the Coca compatibility test for direct matching²¹ We have not seen any untoward reactions to the injection of the dissolved, processed plasma

CONCLUSIONS

(1) Experimental shock was produced by cooling the peritoneal cavity of dogs In this type of shock there is an excessive loss of plasma protein from the circulating blood, and albumin constitutes the major portion of this loss

(2) Preserved plasma was compared with whole blood, saline and acacia in the treatment of this type of shock The plasma was found to be the most efficient therapeutic agent in restoring the normal blood pressure

(3) Plasma was more efficient in treating experimental shock associated with excessive plasma loss than in treating that due to trauma to an extremity

(4) Limited clinical experience indicates that the use of preserved plasma will be of value in the emergency treatment of shock

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THE OPERATIVE TREATMENT OF COMMUNICATING HYDROCEPHALUS

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THERE can, I think, no longer be any doubt concerning the underlying causes of hydrocephalus, nor can there be any instances where the cause of the hydrocephalus cannot be unequivocally demonstrated. The underlying lesions vary greatly in character, but with those rare exceptions where fluid is overproduced, all cause the same effect—namely, an *obstruction* to some part of the system through which the cerebrospinal fluid circulates. The obstruction prevents the fluid from reaching that part of the system where most of the absorption occurs—namely, the subarachnoid spaces over both cerebral hemispheres. Fundamentally, hydrocephalus is not at all different from hydro-ureter and hydronephrosis, or from the effect upon the biliary tracts of stones and other obstructions, which, too, may be quite variable in character, but the effects of the obstructions are the same.

In hydrocephalus, as in other conditions, the obstructions occur in many different locations. When the obstruction closes all or part of the cisternae at the base of the brain, the hydrocephalus is known as *communicating* because the ventricles communicate freely with the spinal canal. When the obstruction closes any part or all of the ventricular system the type of hydrocephalus is called *noncommunicating* because the ventricular system, or the affected part, does not communicate with the spinal canal. The differentiation between these two major types of hydrocephalus is all important from the standpoint of surgical therapy because two fundamentally different anatomic set-ups exist. When the ventricles do not communicate with the spinal canal (and the obstruction is in the ventricular system), it may be assumed that the cisternae are open and that it is only necessary to sidetrack the fluid which may then enter the cisternae and thence be passed along to the subarachnoid space for absorption. (This presumption is by no means always correct, for not infrequently more than one congenital obstruction exists.) But when the *cisternae* are blocked there is no way by which fluid can be made to enter the subarachnoid spaces to be absorbed. There are indeed many instances of communicating hydrocephalus in which the crucial part of the cisternae—the cisternae interpeduncularis and chiasmatis from which all the subarachnoid spaces radiate—are beyond the obstruction, but whether, since they have never contained fluid, they are still potentially patent and could receive fluid from an opening in the floor of the third ventricle is difficult to determine. At any rate there is no safe way of separating this group from those in which the entire length of the cisternae or at least the important anterior half (the cisternae interpeduncularis and chiasmatis) is included.

This being true, for the present, at least, all cases of communicating hydrocephalus are considered alike. The cure of this type of hydrocephalus cannot (except perhaps in some of the isolated exceptions noted above) be accomplished by sidetracking the fluid to any location where great absorption can occur. This being true, the only hope must be in reducing the amount of cerebrospinal fluid that is formed.

Twenty years ago the writer¹ proposed a procedure by which the large glomus of the choroid plexus was removed from both lateral ventricles. It was hoped that the absorption of fluid that occurs in the spinal and cerebellar subarachnoid spaces might take care of the fluid that formed from the remaining choroid plexuses. I have had several undoubted cures resulting from this procedure. It has been my impression that the cures have been principally, though not entirely, in the older infants, where the size of the head was somewhat fixed and the hydrocephalus was, therefore, progressing at a slower pace. That the rate of growth of the head in hydrocephalics is very variable is well known. It has also been my impression that those with the larger choroid plexuses and those with more histologic evidence of obliterations of the vessels in the choroid plexus did better following the removal of the plexuses. It has also seemed that there is a relationship between the histologic degenerative changes in the choroid plexus—which are often profound—and the rate at which the hydrocephalus grows. In effect, the latter changes are the equivalent of partial removal of the plexus.

The purpose of this communication is to show the effect of further operative removal of the choroid plexus from the brain when removal of the glomus from both sides has been found to be inadequate. Since the brain is so rapidly destroyed by advancing hydrocephalus, it is important that delay be avoided when further surgical efforts are to be instituted. One cannot, therefore, wait very long to determine that the earlier operation has been inadequate. In this connection it should be emphasized that unless hydrocephalics are brought very early for treatment, attempted cures are not worth while. There is no point in curing or attempting to cure a baby that is certainly going to be subnormal mentally. For the rapidly growing hydrocephalics, three months is the outside limit for surgical intervention, for those that are growing less rapidly, the limit may vary from six months to a year, all depending, of course, on the actual size and rapidity of the growth of the head. But the earlier the treatment the better the results, both in terms of life and of subsequent mentality.

The surgical procedures that are herewith suggested, and which were carried out with apparent success in one patient, are (1) The cauterization with or without removal of the choroid plexus lying in the posterior cranial fossa—namely, that in the fourth ventricle and along both flocculi (Fig 1 [B and b]), and, (2) cauterization of the plexus in the bodies of both lateral ventricles (Fig 1 [C, c and c']). These procedures are in addition to the routine removal of the glomus and the plexus in the descending horn of both lateral ventricles.

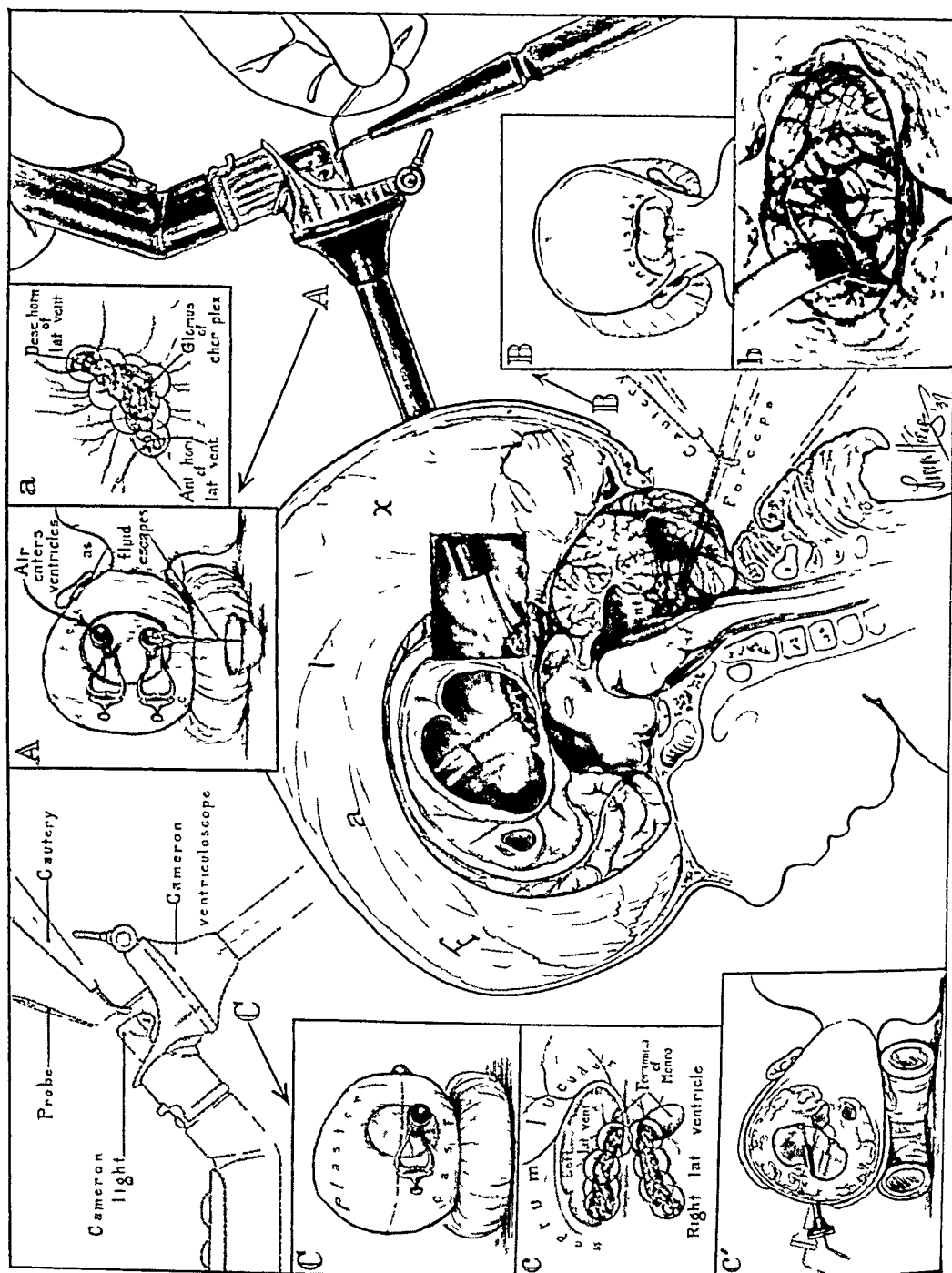


FIG. 1.—Composite drawing. Center showing sites at which the choroid plexus is cauterized and removed (A and a). The glomus of the choroid plexus of each side (B and b). The choroid plexus in the posterior cranial fossa (C and c). The choroid plexus from the body of each lateral ventricle (C' and c').

CASE REPORTS

Case 1—P G, female, age one year, was admitted to the Johns Hopkins Hospital April 8, 1936, with the history that four days before birth the mother had been operated upon for appendicitis. Mother and baby remained in the hospital for nearly three months. At the age of five or six weeks the head was definitely oversize and had since continued to grow, though the rate of growth has not been even. At times it would appear to grow very rapidly and again the increase would be much less. At the age of three months she could hold up the head and even despite its great enlargement she was able to sit up. The head was fairly symmetrically enlarged and measured 54 cm in circumference. The anterior fontanelle was very large, measuring 9x8 cm. The posterior fontanelle was closed. The veins of the scalp stood out prominently. The baby weighed 9,700 Gm.



FIG 2—Case 1. Patient one and one half years following removal of both glomi, the plexus from the posterior cranial fossa and, finally, from the bodies of both lateral ventricles.

The phenolsulphonephthalein test showed free communication between the spinal canal, into which the dye was injected, and the ventricular system. The cerebral cortex was perhaps $\frac{3}{4}$ cm thick.

Operations—April 11, 1936. *Removal of glomus from the right lateral ventricle.* It was first thoroughly coagulated, then removed.

April 17, 1936. *Coagulation and removal of glomus of left lateral ventricle.*

April 28, 1936. *Coagulation of choroid plexus on under surface of vermis at the foramen of Magendie and the prolongation of the choroid into each lateral recess.* There was quite a mass of plexus at each terminus, this was similarly destroyed with the cautery.

June 30, 1936. Patient returned because of vomiting. The circumference of the head was unchanged but the fontanelle was somewhat tense. Through a small opening in the right side of the anterior fontanelle the ventriculoscope was introduced into the anterior horn of the large right ventricle and the choroid plexus was quickly cauterized.

from the foramen of Monro to the scar marking the removal of the glomus The septum pellucidum, curiously, was everywhere intact An opening was cut through this structure by the cautery, and the *plexus of the left lateral ventricle was destroyed with the cautery precisely as on the right side*

The baby was discharged from the hospital July 19, 1936

Subsequent Course—The baby was next seen one year later (July 8, 1937) At that time it was holding up its head, and appeared bright The mother says it understands much that she says to it

The circumference of the head was 57 cm The anterior fontanelle was reduced to 4.5 cm in the anteroposterior diameter and 7 cm in the lateral

The last visit was January 15, 1938, one and one-half years after the operation The head measured 57 cm in circumference, the anterior fontanelle 5.5 x 2 cm (Fig 2) The baby looks bright, sees and is beginning to talk Both arms and legs are used freely When lying on her stomach she raises her head and looks from side to side She plays with her toys all day long, she loves to listen to the radio She has made no effort to get on her feet

This series of operative procedures had been carried out in another child, age five months, a year previously, the patient died, however, six weeks following the final operation, too soon to estimate upon the effects of it on the hydrocephalus

In this connection the results on a third little patient are of interest because pathologic considerations prevented the attempted removal of the choroid plexus from the posterior fossa, and cauterization of that in the bodies of the lateral ventricles has so far been withheld, but the little baby is, at the end of eight months, seemingly well and apparently cured

Case 2—R H, male, age three months, was admitted to the Johns Hopkins Hospital, with the history of having had a difficult birth The head was thought to have been large at that time, the mother, however, was reported to have had a contracted pelvis The baby was delivered with instruments It cried feebly but took its feedings by the breast immediately after birth It was not until the end of the ninth week that Dr C Rosenberg of Newark, N J, observed the first evidence of hydrocephalus (Fig 3)

Examination—Except for the enlarged head the baby was well developed, well nourished and looked healthy The head was markedly enlarged, measuring 50 cm in circumference, the anterior fontanelle measured 6 x 6 cm The veins of the scalp were dilated

Operations—June 12, 1937 The glomus of the choroid was removed from both lateral ventricles at one operation The cauterization was continued down both descending horns and for some distance along the body of the ventricles The cerebral hemispheres were not more than 1 cm thick at the site of the ventricular openings The ventricular fluid was strongly colored with phenolsulphonephthalein that had been introduced into the spinal canal on the preceding day

June 25, 1937 Assuming that further operative treatment would be necessary, a bilateral cerebellar exploration was made Cauterization of the plexus in the posterior cranial fossa was intended However, there was a very dense scar at the foramen of Magendie which was tightly sealed and the cerebellar tonsils projected slightly into the spinal canal Hoping to reach and remove the choroid plexus within the fourth ventricle, the vermis was split and an opening that would admit the index finger was made into the large fourth ventricle The incision was carried posteriorly to the medulla in the midline The choroid plexus could not be seen, it was all incorporated within the scarred mass and was beyond reach Since the hydrocephalus was clearly of the com-

municating type, the opening into the fourth ventricle could play no part in the subsequent cure of the hydrocephalus

Subsequent Course—This little patient was last seen November 15, 1937—five months after the first operation (Fig 3 [A and B]) It was a very normal looking baby with bright eyes, it was cooing and playful Its head had increased only 1 cm since the admission to the hospital—a normal rate of growth The anterior fontanelle now measured 5×2 cm, a reduction of 1×4 cm, it was neither tight nor bulging A letter received February 1, 1938, stated that the baby continued to thrive, was seemingly normal and measurement of the head showed no increase

A

B



FIG 3—Case 2 (A) and (B) Five months after the removal of glomus from both lateral ventricles An attempt was made to remove the plexus from the posterior cranial fossa, but it could not be reached because it was incorporated in a dense scar

Cauterization and Removal of the Glomus—Preparatory to this and all the other operative procedures upon hydrocephalic children whose sutures have not united, it is necessary to fix the head in a plaster encasement If this is not done, the head will collapse as the fluid escapes, and collapse of the head is almost necessarily fatal

I always prefer to attack the choroid plexus through an air medium because it is much more simple (Fig 1, center), the plexus is so much better seen and so much easier of cauterization and removal I have tried the various water cystoscopes used by Dr Hugh Young, and with special improvements for the local situation, but have never been able to get results as satisfactorily as with the air medium Working in an air medium, one has a far sharper, clearer view, never obscured, as in a water medium, by any little bleeding, moreover, any bleeding points can be promptly controlled either with cotton pledgets or the electrocautery

The cutaneous incision is straight and vertical (about 2 cm in length) in the occipital region of each side and about 2½ to 3 cm from the midline (Fig 1 [A]) The bone is rongueured away until its opening is almost exactly the size of the small ventriculoscope After opening the dura and cauterizing any cortical vessels, the underlying cortex is incised and the ventriculoscope

is introduced into the posterior horn of the ventricle (Fig 1 [A]) The ventricular fluid is collected, kept warm and replaced at the end of the operation After much experimentation the Cameron light has been found to be much the most satisfactory The illumination of the ventricle is almost perfect and without sacrificing room in the tube In order to prevent the effects of the electrocautery from spreading, an insulated German bakelite tube is used Prior to the use of this ventriculoscope I used a headlight of German make and from which parallel rays of light passed down the narrow tube, although very satisfactory, it was not so simple, in that frequent adjustments of the head mirror were necessary to attain the exact angle for passage of light down the ventriculoscope

In recent years I have usually, but not invariably, removed the glomus of only one ventricle at a time (Case 2 is an exception) It is so easy to remove both at a single operation that it is tempting to do so, but there is no doubt that it carries a higher mortality Usually an interval of a week between the right and left sides is sufficient It is worthy of note that when the head is in a plaster encasement, rapid removal of the ventricular fluid has no effect upon the baby's pulse, respirations or color Such changes are very promptly induced by even a slight loss of blood The best method of attack upon this mass of dangling choroid plexus—the glomus—has also been determined only after much experimentation It can be aspirated (only in young babies) into a continuous suction tube very easily and with scarcely any bleeding because the vessels of this age are small and contract promptly However, it is probably preferable to cauterize the mass by applying a metal probe to its surface until it is greatly shrunken (Fig 1, center) This mass can then be removed with long slender bladed forceps, or sucked through the tube, or even left in place Every effort is made to cauterize that portion of the choroid plexus that passes to the tip of the descending horn and also that in the body of the lateral ventricle, from this point of attack one can rarely cauterize the plexus far beyond the bend into the body of the ventricle

Before withdrawing the ventriculoscope, the ventricular fluid is replaced and any deficit is supplied by Ringer's solution Since the ventriculoscope is accurately applied to the dual defect and the opening in the cortex, air cannot pass outside the cortex and cause it to collapse It might be supposed that fluid would subsequently pass through the cortical opening and collect outside the cerebral cortex, causing it to collapse, but this does not happen when the cortical opening is small In fact, this opening soon heals over and in the course of time can scarcely be found It is, of course, obvious that these openings are made in a silent part of the cerebral cortex Conceivably the visual cortex might be injured, but I have not seen this happen

Removal of the Choroid Plexus in the Posterior Cranial Fossa—There is quite a volume of choroid plexus in the posterior cranial fossa Usually the cisterna magna, the foramen of Magendie and the fourth ventricle are all exceedingly large in communicating hydrocephalus Exposure of the posterior cranial fossa by a small bilateral suboccipital craniotomy brings all of the

choroid plexus in this region immediately into view (Fig 1 [B and b]) Even the extension of the choroid plexus laterally into each lateral recess is directly visible because the large cisterna magna extends laterally around the brain stem and lifts the cerebellum upwards as far as the inferior peduncles, under which the choroidal extensions pass to the foramina of Luschka (Fig 1 [b]) where they form a mass comparable to, but smaller in size than, the glomus of the lateral ventricles It requires only a few minutes to completely cauterize all of the choroid plexus in the posterior cranial fossa As the choroid passes along the vagus nerve the cauterization must be cautiously performed to avoid dysphagia This actually resulted in this little patient but cleared after several days

There are exceptions to the above topographic relations At times the foramen of Magendie is closed and the fluid must then escape through the ventricles through the lateral foramina of Luschka Under these conditions the cisterna magna may be very small and the cerebellum snugly applied to the brain stem, thus completely hiding and making difficult or impossible of exposure the entire mass of choroid plexus in the posterior fossa In the second case of this report this situation was encountered The cerebellum was tightly bound to the medulla everywhere and the foramen of Magendie was closed by a dense scar so that neither the lateral extensions of the choroid nor that in the fourth ventricle could be safely reached I am not prepared to say that many cases of hydrocephalus cannot be cured without including this portion of the choroid plexus in the sum total that is extirpated or necrosed, but the evidence at hand appears to indicate that it is essential in many

Cauterization of the Choroid Plexus in the Body of Each Lateral Ventricle—Extirpation of the choroid plexus from the bodies of the lateral ventricle is not possible because the plexus is but slightly elevated However, it is only necessary to lightly draw the coagulating needle of the electrocautery (or better a probe which is touched by the cautery) along it (Fig 1, center) from the scar at which the glomus has been previously removed posteriorly to the foramen of Monro, to see it shrivel to a white streak It has seemed better to coagulate this part of the plexus on both sides at a single sitting, first because it is necessary to remove only about two-thirds of the ventricular fluid, second, because the amount of cauterization is less than elsewhere, third, because of the desire to avoid entry through the more important left hemisphere, and finally, because both sides can be reached almost as easily as one (Fig 1 [c']) To accomplish this end the same sized Cameron ventriculoscope is passed through the right side of the anterior fontanelle, which is always large The air medium is also used in the attack upon this part of the plexus Usually the septum pellucidum is already perforated, or even largely destroyed by the pressure of the hydrocephalic fluid It is then only necessary to shift the ventriculoscope through the openings to expose the choroid plexus on the left side (Fig 1 [C']) But if no perforation exists, as in the above case, one of adequate size can easily be incised with the cautery

Summary and Conclusions—In the treatment of communicating hydrocephalus the removal of the glomus from each lateral ventricle may or may not be sufficient to produce a cure. If not adequate, additional choroid plexus may be removed or destroyed by the cautery. (1) From the posterior cranial fossa (fourth ventricle and lateral recesses), and/or, (2) from the bodies of both lateral ventricles. Only experience and careful study of the effects of each attack can tell when the added removal is necessary. There is so much individual variation in the rate of growth of hydrocephalus that no set rule can indicate beforehand whether additional removal is necessary, and if so, how much. Since most cases do require more than the removal of the glomus, I am inclined to destroy the plexus in the posterior cranial fossa (when this is possible) without waiting to see the effects of removal of the glomus. By so doing the extensive destruction of brain tissue in the unsuccessful cases may be avoided.

The test of success or failure of these operations is, to a very large extent, dependent upon measurements of the head, and by the time it is known that the operation has not been successful, extensive destructive of the brain tissue has resulted, which may well mean the difference between a subsequent normal and impaired mentality. Nothing should be left undone to insure, when possible, the minimum of cerebral damage. By and large, the destruction of brain tissue is far more serious than the risk of the added operation.

The final suggested attack, namely, cauterization of the plexus along the bodies of both lateral ventricles, should, I feel, be left until it is definitely demonstrated that both of the other procedures have been inadequate.

Admittedly each of the above operative procedures is one of magnitude and is fraught with danger, but when the hydrocephalus of the communicating type continues to progress, there appears to be no alternative. It seems impossible that this type of hydrocephalus can be cured except by the removal of a sufficient amount of choroid plexus. In the case here reported and the one that died subsequently, it was only the continuation of pressure, as indicated by a tense fontanelle and vomiting, that made the need of the last choroid plexus removal necessary (from the bodies of the lateral ventricle), if this line of attack were going to be successful. Only the choroid plexus in the roof of the third ventricle remains, and even the beginning of this at the foramina of Munro has been included in the cauterization. Even this could be removed very simply by splitting the corpus callosum, but it is difficult to believe that this small remaining amount of plexus could maintain a progressive hydrocephalus of this type.

REFERENCE

- ¹ Dandy, Walter E. Extirpation of the Choroid Plexus of the Lateral Ventricles in Communicating Hydrocephalus. *ANNALS OF SURGERY*, 68, 569, 1918

PRIMARY MALIGNANCY OF THE JEJUNUM AND ILEUM*

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THE MATERIAL upon which this paper is based consists of four cases of primary malignancy of the jejuno-ileum which I have observed during the last eight years, and the reports in the literature during the same period of time of 196 similar cases (Table I) These tumors are rare and unusual Individual experience has rarely exceeded and seldom equaled a half dozen observations Carcinomata, malignant carcinoids and sarcomata comprise these malignancies Other reported types may be excluded because of their negligible incidence or questionable origin

Carcinomata outnumbered sarcomata 5 4, and malignant carcinoids 8 1 The average age incidence for these three groups is respectively 51 48 and 57 years, exclusive of infants and children, who comprise 10 per cent of the sarcoma group, and who are almost exclusively males

Primary malignancy does not respect any part of the jejuno-ileum It attacks the extremities with the greatest frequency, but is found in the intervening portion in one-third of instances The proximal fourth of the jejunum and the distal fourth of the ileum account for 40 and 28 per cent of occurrences respectively The carcinomata predominate in the former, and the sarcomata in the latter location The malignant carcinoids manifest a marked preference for the ileum, particularly its terminal portion (Table II, Fig 1)

Multiple carcinomata occur very rarely, but one-sixth of the malignant carcinoids and half as many of the sarcomata exhibit plural sites of origin Carcinomata are predominantly of the adenomatous type, and may appear

PRIMARY MALIGNANCY OF THE SMALL BOWEL

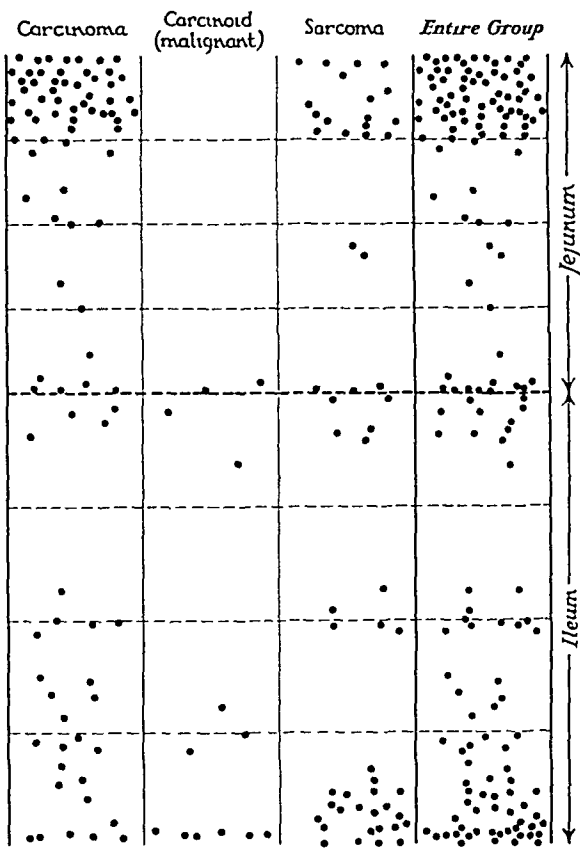


FIG 1 —Scatter chart illustrating the locations of the primary malignant tumors of the jejuno-ileum

* Read before the Western Surgical Association at Indianapolis, Ind, December 3, 1937 Submitted for publication January 24, 1938

TABLE I

CASE REPORTS OF PRIMARY MALIGNANCY OF THE JIJUNOHIUM COLLECTED FROM THE
LITERATURE SINCE 1930

Author	Carci- noma	Carci- noid	Sar- coma	Author	Carci- noma	Carci- noid	Sar- coma
Ackman, F D	7		5	Goldsmith, R			1
Appelmans, R, and Picard, E	6			Gotten, H B	4		4
Bagozzi, U Clerici			1	Gray, H K, and Kernohan, J W	1		
Bagnaresi, G			1	Gray, J			2
Bailey, O T		2		Greenfield, H			1
Baldwin, J F				Harries, J D, and Harrison, C V	2		
Barnhart, S E	1			Harris, F I, and Rosenblum, H	1		
Bartlett, M K	1			Hartman, H R	1		
Bollag, L	1			Hodges, F C, and Vest, W E			1
Bowers, J M, and Mullen, B P	1			Hodgkins, E M	2		
Brink, J R, and Laing, G H			1	Hortolomei, N, and Butureanu, W			1
Brown, R	1			Jonas, E, Steck, E L, and Brams, J	1		
Buscke, H J			2	Joyce, T M	3		
Cabot, Case 22262	1			Kiefer, E D	8		1
Cabot, Case 23111			1	Klopp, E J, and Crawford, B L			2
Carter, R Franklin	5			van Knorre, G			1
Cave, H W	7		3	Kordenat, R A	1		
Charlier, M André	1			Koucky, R W	1		
Charache, H			1	Lanos, J	1		
Charleux, G, and Cuny, J			1	Leriche, R, and Brun, M			1
Cooke, H H		3		Liccione, W T			1
Cox, W			1	Lingley, J R	1		1
Crousse, R			2	Lynch, J M	1		
Cuny, J			1	Magnusson, R			1
DeCaestecker			3	Malerich, J A	1		1
Doub, H P, and Jones, H C		2		Matsubara, I			
Duperie and Mau- petit			1	Mayo, C W, and Robins, C R, Jr			1
Eckhardt, J J			8	McDermott, J G			1
Faust, Louis S, and Walters, W			1	Michael, P, and Bell, H G	1		
Finkelstein, R, and Jacobi, M	1			Mitchell, E W	1		
Finsterer, H			3	Moore, G A	1		
Foged, J	1			Mumey, N			2
Franke, K	2			Nettrour, W S	1		
Gabor, M E, and Hiller, R I	1			Newton, A	1		
Gaspar, I		1					
Goldberg, S A	2						

Author	Carci- noma	Carci- noid	Sar- coma	Author	Carci- noma	Carci- noid	Sar- coma
Newton, F C , and Buckley, R C	2			Soubeiran, M	1		
North, J P	2		1	Suris, Sola			1
Oetelle, E			1	Sussi, Luigi	1		
Palumbo, E	1			Taylor, E H			1
Plunkett, J E , Foley, M P , and Snell, A N	1			Udie			1
Porzelt, W	1			Ullman, A , and Abe- shouse, B S			1
Pow, D L	1			Wakeley, C P G , and Paul, M A	4		3
Proescher, F , and Muir, J	1			Warren, S , and Gates, O		1	
Raiford, T S	1	2	3	Weinstein, M			1
Rankin, F W , and Donald, J M	1			Wellbrock, W L A	1		
Ritchie, G		1		Whitaker, L , and Fisher, J H			1
Ross, K	2			Williams, O H , Wil- hams, W R , and			
Rowe, E W , and Neely, J M	5		2	Mole, R H	2		
Schlachetzki, H	1			Wiseley, A N	1		
Scholte, A J		1		Wood, W G		1	
Sowles, H K	5			Totals	109	12	75

TABLE II
LOCATION OF MALIGNANT NEOPLASMS OF THE JEJUNO-ILEUM

Type of Tumor	Jejunum	Ileum	Undetermined	Total
Carcinoma	70	35	4	109
Malignant carcinoid	1	12		13
Sarcoma	33	42	3	78
Total	104	89	7	200

as a simple ulcer, a papillary growth or an annular, ulcerated constriction. The malignant carcinoids, until recently, were confused with the carcinomata, from which they are readily distinguishable by microscopic examination alone, without the aid of silver or other special stains. Histologic examination fails, however, to reveal their malignant properties, evidence of which must rest upon metastasis or invasion, unless it is assumed that all small bowel carcinoids are malignant. These malignant neoplasms assume a nodular or sessile form, rarely do they involve the whole circumference of the bowel. They usually compromise its lumen, either through intraluminal encroachment or by a puckering distortion of the bowel wall in contradistinction to a complete ring-like stenosis. Mucosal ulceration is not infrequent.

The sarcoma group is classified here as fibrosarcoma, leiomyosarcoma and malignant lymphoblastoma, the latter is of lymphoid tissue origin and includes lymphosarcoma, Hodgkin's disease of the intestine and reticulo-endothelioma (Table III) Microscopically, these three types of lymphoid tumors frequently blend in borderline cases so as to render impossible a hard and fast classification in all instances Only one-third of the sarcomata are of connective tissue or smooth muscle type, two-thirds of this group are of lymphoid structure, of which the lymphosarcoma accounts for four out of five cases

TABLE III

CLASSIFICATION OF THE SARCOMATA OF THE ILEUM-ILLUM

	No of Cases
Fibrosarcoma	10
Leiomyosarcoma	9
Malignant lymphoblastoma {	
Lymphosarcoma	43
(Hodgkin's disease of the intestine)	4
Endothelioma	2
Unclassified	10
Total	78

The sarcomata manifest such striking and numerous individual variations as to render futile any attempt at a general descriptive statement One-fourth are large and one-fifth are adherent to some neighboring viscus, usually the colon They exhibit large and small extraluminal and intraluminal masses, also large and small annular formations with and without narrowing or obliteration of the lumen A peculiar type of growth characteristic is the transformation of an appreciable length of small bowel into a hard, rigid thick-walled tube

Carcinomata, malignant carcinoids and sarcomata are all capable of producing bowel obstruction, the first two with an average frequency of 90 and 80 per cent, respectively, 56 per cent of the sarcomata produce this complication, which is nearly always mechanical, regardless of the kind of tumor The carcinomata and malignant carcinoids are primarily constrictors Intraluminal encroachment and extraluminal occlusion are produced less frequently by these growths Sarcomata obstruct usually (1) In the form of large or small annular masses, (2) by the formation of a rigid tubular segment, and (3) by intussusception and less frequently by (4) intraluminal encroachment, (5) extraluminal compression, and (6) angulation of the bowel wall due to matted and adherent coils of intestine

There is a peculiar type of annular sarcomatous growth which causes dilatation of the bowel lumen instead of constriction It has been emphasized

more than its incidence warrants, with the result that there is widespread belief that such a deformity represents the usual type and that sarcomata of the bowel rarely produce obstruction. Actually, constricting sarcomatous growths occur three times more frequently.

Metastases have been discovered at operation in approximately one-fourth of the carcinoma and sarcoma cases, and at autopsy in approximately 90 per cent. They may be widespread but are seldom found outside the abdomen. The regional mesenteric lymph nodes and the liver bear the brunt of these deposits. As would be expected from our definition of a malignant carcinoid, practically all have metastases at operation and autopsy.

The symptoms vary greatly in kind and degree in the same and different individuals. They are determined by such factors as the size, location and extent of the primary and possible secondary growths, and whether or not intestinal obstruction is present. With few exceptions, with or without obstruction, the complaints are referable to the abdomen and to the gastrointestinal tract. Infrequently, the manifest symptoms of small bowel involvement are absent or are so mild as to be overshadowed by other primary or secondary ailments.

The onset of symptoms may be sudden and severe, as in perforation, intussusception or sudden occlusion, usually they are insidious and frequently consist of anorexia, dyspepsia, weakness, fatigue and vague abdominal discomfort. Loss of weight and constipation are pronounced in most instances. Diarrhea occasionally occurs. Alternating constipation and diarrhea are frequently present. Occasionally a massive bowel hemorrhage occurs which originates surprisingly often in a tumor of the connective tissue or smooth muscle types, the leiomyosarcomata are the chief offenders in this respect. The patient infrequently observes evidence of blood in the stool. Occasionally he discovers an abdominal tumor, which is usually a large sarcoma. Rarely are the smaller carcinomata and malignant carcinoids found by the patient.

The duration of symptoms varies from a few hours to several years. It is usually expressed in terms of months. Approximately one-half of the cases have had symptoms for six months or less, and three-fourths for one year or less.

The physical findings may or may not be abnormal. They are conveniently classified as general and abdominal. The positive general findings are usually indicative of a wasting ailment and consist of pallor, fever, undernourishment, emaciation and cachexia of various degrees and combinations. Their incidence is slightly under 20 per cent for carcinomata and somewhat higher for sarcomata.

The positive abdominal findings are for the most part those of chronic obstruction and tumor, and seldom are of an acute abdominal condition. The instances of acute obstruction and perforation are relatively few. The percentage incidence of palpable sarcomata is high and exceeds greatly that of the carcinomata, the respective values are 65 and 29 per cent. The diameters of half of the sarcomata equal or exceed 5 cm. These tumors not

infrequently are large or massive. The carcinomata, on the other hand, are usually small and seldom, if ever, massive, they rarely attain a diameter of 6 cm.

Intestinal tumors are usually movable but may become adherent and immovable, this is especially noteworthy of the sarcomata, which are often attached to surrounding structures.

The hemoglobin values are appreciably low in most instances but only occasionally are they under 50, such extreme depletion is usually found in an illness of long duration, or in one characterized by a sudden severe hemorrhage. The stools may or may not contain evidence of blood. Occasionally the latter is present in enormous amounts.

Röntgenologic observations are extremely valuable in the determination of the presence, degree and level of an obstruction, and also for revealing the relationship to the bowel of an abdominal tumor, negative as well as positive findings are important. The evidence of obstruction infrequently justifies an expression of opinion regarding its nature. The scout film, colon depiction after an opaque enema, and a specially executed gastro-intestinal examination after the ingestion of barium, comprise the roentgenologic procedures usually employed. The serial films and observations must be taken at frequent intervals to obviate missing transitory evidence of obstruction and alterations in bowel wall contour. The hazards of a barium meal in the presence of severe obstruction are well known and frequently contraindicate its employment. The scout film was rarely employed in this series, and the barium enema very infrequently. Because of their great merit this constitutes a serious omission. Gastro-intestinal studies were carried out in 46 per cent of instances.

A 20 per cent error prevailed in the recognition of actual obstruction. Neoplastic involvement was suspected in 25 per cent of instances of recognized obstruction. The possibility of exact clinical diagnosis does not exist. Rarely is a diagnosis of any kind of primary neoplastic disease of the jejunum-ileum well founded. Usually diagnostic resources are exhausted in the recognition of an obstructive lesion primary in the small bowel. With rare exceptions, only obstructive cases disclose evidence indicative of possible primary neoplasia, this obstructing group comprises approximately three-fourths of the total number of tumors under discussion.

The significant diagnostic factors are the history, physical, laboratory and roentgenologic evidence, of which the history and roentgenologic evidence are the most uniformly positive and suggestive, the former is almost never negative, and the latter never. In other words, positive roentgenologic evidence of small bowel alteration is indispensable in all instances. Positive physical findings such as a palpable tumor and positive laboratory findings, such as blood in the stool, are always significant, but never essential. Diagnostic accuracy is greatly enhanced when all four factors are positive and mutually supportive.

The nonobstructive cases present almost insurmountable diagnostic dif-

difficulties Two recent reports indicate conclusively, however, that a correct diagnosis of a primary small bowel tumor is possible, at times, even in these cases They both concerned palpable tumors with central cavitation, whose small bowel origin was proved by the roentgenologic evidence of the air filled cavities, into which ingested barium flowed The bowel lumen of the resected segment was found to be dilated within the tumor

In this series one-sixth and one-seventh, respectively, of the carcinoma and sarcoma cases were diagnosed correctly insofar as the presence of a primary, small bowel tumor is concerned In some instances the diagnosis was not warranted by the evidence In a few cases malignancy was suspected and diagnosed correctly upon roentgenologic findings of infiltration of the bowel wall by a tumor

Radical surgical removal in one or more stages is the basis for cure, and was performed with this object in view in 69 and 64 per cent, respectively, of the carcinoma and sarcoma cases, only three of the 13 cases of malignant carcinoid received similar treatment

Postoperative roentgenotherapy is administered frequently, particularly in instances of sarcoma Palliative operations to relieve obstruction are occasionally performed, and sometimes are as extensive as the curative procedures

The prognosis is unsatisfactory with respect to both the immediate operative mortality, which is 30 per cent, and the ultimate results, there is no noteworthy difference in the outcome of the first few years between the carcinoma and sarcoma cases, which show respective percentage survival at one year of 24 and 30, and at three years of 13 and 10 per cent, the respective values at five years are six and ten One carcinoma case and one of malignant carcinoid lived eight years, the latter being the author's case Three sarcoma cases survived operation eight years, two 13 and one 20 years

Metastasis was found upon microscopic examination of the removed tissue in one of the five carcinoma cases who survived operation five years, and also in the author's case of malignant carcinoid, like evidence was disclosed in only one of the six sarcoma cases who survived an equal length of time This single occurrence was in another of the author's cases Of these latter six cases of long survival two were fibrosarcomata, one leiomyosarcoma, and three lymphosarcomata Only one received roentgenotherapy The leiomyosarcoma case died of a recurrence 13 years and eight months after operation The 20 year survival was that of an instance of fibrosarcoma (Table IV)

CASE REPORTS

Case 1—L. P. M., female, age 48, was first seen March 17, 1930, because of a diarrhea of 18 months' duration, 30-pound loss of weight, occasional generalized abdominal distress and two recent attacks of severe abdominal pain, accompanied by nausea, vomiting, and blood stained stools

The physical findings were negative upon entrance The laboratory examinations

TABLE IV

MORTALITY AND SURVIVAL DATA OF OPERABLE CASES

	Carcinoma		Carcinoid		Sarcoma	
	No	Percentage	No	Percentage	No	Percentage
Operable	75	69	3	23	50	64
Immediate mortality	22	29 $\frac{1}{3}$	0	0	15	30
Alive six months	25	33 $\frac{1}{3}$	2	66 $\frac{2}{3}$	17	34
Alive one year	18	24	2	66 $\frac{2}{3}$	15	30
Alive two years	13	17 $\frac{1}{3}$	1	33 $\frac{1}{3}$	7	14
Alive three years	10	13 $\frac{1}{3}$	1	33 $\frac{1}{3}$	6	12
Alive four years	6	8	1	33 $\frac{1}{3}$	6	12
Alive five years	5	6 $\frac{2}{3}$	1	33 $\frac{1}{3}$	6	12
Alive six years	2	2 $\frac{2}{3}$	1	33 $\frac{1}{3}$	6	12
Alive eight years	1	1 $\frac{1}{3}$	1	33 $\frac{1}{3}$	3	6
Alive 13 years	0	0	0	0	2	4
Alive 20 years	0	0	0	0	1	2
Not stated	17	22 $\frac{2}{3}$	1	33 $\frac{1}{3}$	8	16

showed Blood Wassermann, negative, hemoglobin, 15.3 Gm, erythrocytes, 4,485,000, leukocytes, 7,350, stools negative for blood. A gastro-intestinal study following a barium meal was negative.

Following two attacks of severe abdominal pain during the first five weeks of

FIG 2



FIG 3



FIG 2—Case 1. Low power photomicrograph of malignant carcinoid of ileum, showing a dense fibrous stroma infiltrated with characteristic epithelial cell masses, with no tendency to tube formation.

FIG 3—Case 1. High power photomicrograph of a metastatic carcinoid deposit in a mesenteric lymph node. This shows the characteristic masses of small cuboidal epithelial cells, with regular deeply staining nuclei.

hospitalization, there developed fever, leukocytosis, bloody stools and findings indicative of an acute inflammatory peritoneal involvement

During the second attack an exploratory celiotomy was performed, which disclosed a mesenteric tumor 7 cm in diameter, together with torsion of the mesentery from right to left, with resulting gangrene of several feet of distal ileum. A resection of 160 cm of ileum with a large part of its adjacent mesentery was carried out, and was followed by a lateral anastomosis. An uneventful recovery occurred. Diarrhea persisted for one year. The patient is living and well (April, 1938), eight years postoperative.

The mesenteric tumor upon section presented a yellow, fleshy surface. Upon opening the intestinal segment a small whitish tumor was discovered upon the mucosal surface. It measured 2.5 cm in diameter.

Microscopic examination of these two tumors revealed a moderately dense fibrous stroma, which was diffusely ingrown with huge sheets and cords of epithelial cells showing no tendency to tubular formation. The individual cells were cuboidal or polygonal, with a moderate amount of pink, finely granular cytoplasm and comparatively large spherical nuclei. The diameters of the cells and nuclei were practically uniform. There were no mitotic figures (Figs 2 and 3). The muscularis of the bowel was infiltrated with cords of epithelial cells. *Pathologic Diagnosis* Primary malignant carcinoid tumor of the ileum with metastasis to the mesentery.

Comment—Obstruction produced by primary malignancy of the jejuno-ileum is nearly always of the mechanical type, this case, however, belongs to the strangulating type of obstruction. It is noteworthy that this primary tumor produced no symptoms and was not discovered until a careful examination was made of the resected bowel segment. This tumor belongs to a group of extremely rare small bowel malignancies, whose number in the literature does not exceed 40.

Case 2—S. A., male, age 42, was first seen April 14, 1932, complaining of colicky abdominal pain, nausea, vomiting, anorexia, weakness, 17 pound weight loss and constipation, which symptoms had begun five months previously. He had a 10 year history of gastro-intestinal disturbances. Three years before, an operation was performed for a perforating duodenal ulcer and gallstones, with resulting freedom from symptoms for two years, which ended with the onset of the present disturbances. Temperature, 101° F.

Physical Examination—Weakness and emaciation were pronounced. Upper abdominal distention and visible peristaltic waves, left to right, were present. A small, hard, immovable and tender mass 2 cm in diameter was palpated in the left upper abdominal quadrant. A second smooth, firm, immovable tumor 6 cm in diameter was found in the right lower abdominal quadrant.

Laboratory Data—Blood Wassermann, negative, hemoglobin, 13.2 Gm erythrocytes, 4,210,000, leukocytes, 6,550, stools negative for blood. Gastric analysis after an Ewald meal gave the following values: Free HCl 15, total HCl 28. Gastro-intestinal roentgenologic studies, after a barium meal, revealed a normal stomach and duodenal cap. The second portion of the duodenum was



FIG 4—Case 2. Roentgenogram showing an irregular filling defect at the duodenojejunal flexure, which was diagnosed as a malignant infiltration of the bowel wall. It proved to be Hodgkin's disease of the jejunum.

somewhat narrowed and distorted. A loop of small bowel at the duodenojejunal flexure showed numerous finger-like areas of irregularity, loss of the normal markings and irregular filling defects (Fig 4). The barium passed through this area with but little delay. A tumor was palpated here. There was a 50 per cent gastric retention one hour later. A diagnosis was made of a partially obstructing lesion of the duodenal flexure, most likely a malignant infiltration of the bowel wall. At operation a hard immobile, obstructing tumor about 8 cm in diameter was found in the jejunum at its junction with the duodenum. There was marked regional adenopathy. A second retroperitoneal tumor, 5 cm in diameter, was felt below the lower pole of the right kidney. A palliative posterior gastro-enterostomy was performed. Death occurred 24 hours later, apparently due to surgical shock.

Autopsy—The entire circumference of the proximal jejunum for a distance of 11 cm was found to be involved by a tumor. The mucosa was nodular. This intestinal wall measured 5 cm in thickness. Metastases to the mesenteric lymph nodes were found.

FIG 5

FIG 6

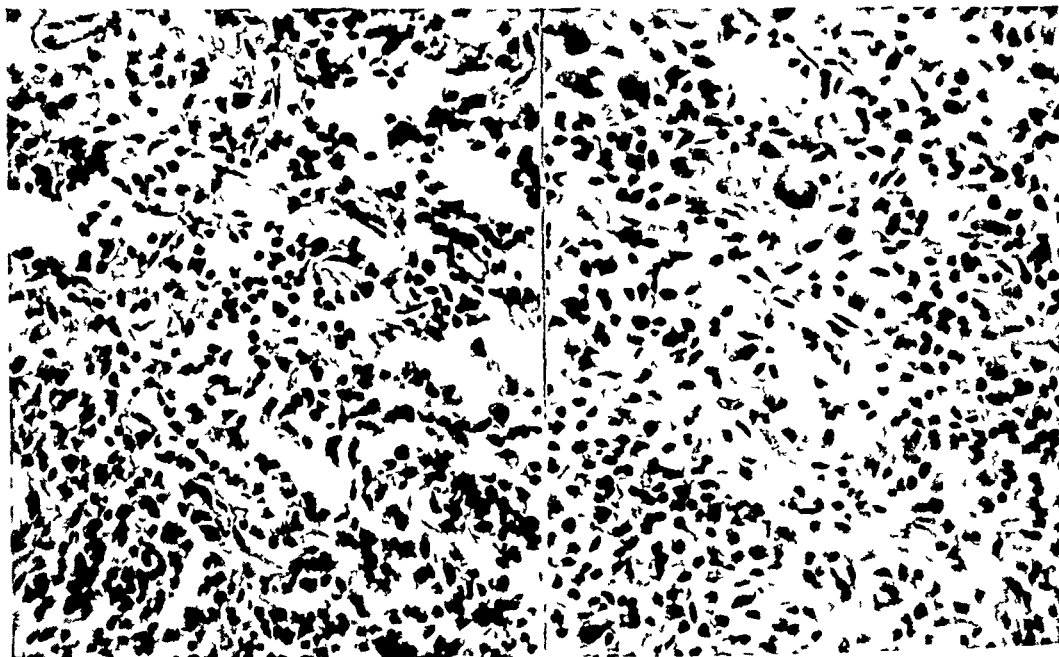


FIG 5—Case 2. Photomicrograph of Hodgkin's disease of the jejunum. The cells are chiefly lymphocytes, but reticulum cells are present also. (High power.)

FIG 6—Case 2. Photomicrograph of a metastatic deposit in a mesenteric lymph node. (High power.)

Microscopic examination of the primary and secondary tumors revealed a rather dense fibrous tissue reticulum supporting masses of small round cells resembling lymphocytes, a few plasma cells, occasional giant cells and large mononuclear reticulum cells with an abundant, finely granular cytoplasm and small round nuclei (Figs 5 and 6). A diagnosis of Hodgkin's disease of the intestine was made. This condition resembles ordinary Hodgkin's disease only in its histologic appearance and malignant manifestation.

Case 3—O O, male, age 48, was first seen January 20, 1932, complaining of colicky abdominal pain, nausea, vomiting, constipation and a weight loss of 24 pounds. These symptoms had been present for six weeks. The first disturbance consisted of quite severe left upper abdominal quadrant colicky pain, appearing soon after the evening meal, and accompanied by nausea and repeated copious vomiting. There was a recurrence of these symptoms four days later and several times subsequently. The stools became hard and dry, because of which laxatives were taken. There were daily movements until the three day period before examination, when there was none. Pro-

gressive pallor had been observed for three months, and constituted the only positive physical finding when first seen

Laboratory Data—Hemoglobin, 9.6 Gm, erythrocytes, 3,860,000, leukocytes, 6,400, blood Wassermann, negative, gastric analysis after an Ewald meal Free HCl 15, total HCl 34. Seven stools gave three positive guaiac tests. Two gastro-intestinal roentgenologic studies after barium ingestion were carried out six days apart, and revealed a normal stomach and duodenum but a slight dilatation of the proximal jejunum above an area of constriction. This constricted area presented the appearance of an infiltrative type of tumor (Fig 7) and was so diagnosed, a carcinoma being suspected because of its relatively greater frequency in this location.



FIG 7—Case 3. Roentgenogram showing the dilated proximal jejunum caused by a constriction, apparently produced by an infiltrative type of lesion, whose level is indicated by the arrow. A roentgenologic diagnosis of primary malignancy of the jejunum was made. The tumor proved to be a lymphosarcoma.

Operation—An annular jejunal tumor was found 47 cm from the duodenojejunal flexure. The proximal jejunal segment was four times larger than normal and its walls greatly hypertrophied. Distal to the tumor were collapsed intestinal coils of normal appearance. The constricting band was 7 cm in width. It was adherent to the great omentum and the descending colon. Three enlarged and quite firm lymph nodes were present in the adjacent mesentery. Forty-six centimeters of the jejunum were resected, together with the adjacent mesentery bearing the lymph nodes and the involved portion of

the anterior wall of the descending colon. This window-like defect of the colon was closed and the jejunal segments were joined end-to-end. An uneventful recovery followed with a rapid gain in weight. The patient left the hospital 15 days after the operation. Shortly afterwards he was given two courses of deep roentgenotherapy. He is living and well six years after operation.

FIG 8

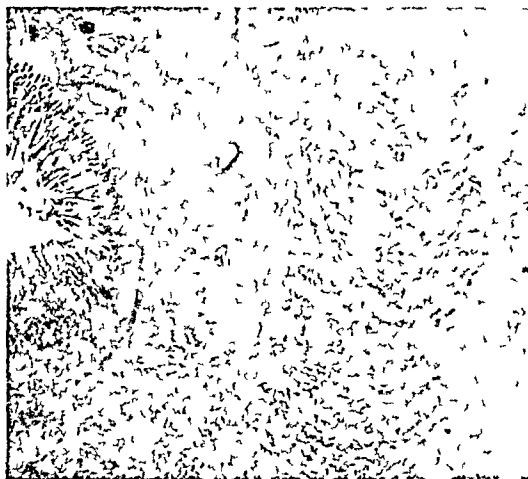


FIG 9

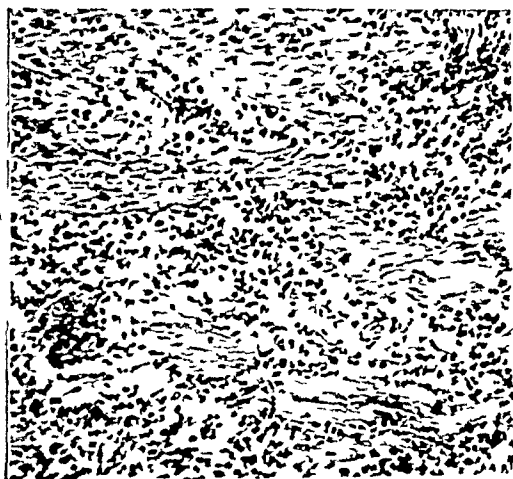


FIG 8—Case 3. Photomicrograph showing the entire thickness of the jejunal wall to be infiltrated with lymphosarcomatous tissue (Low power).

FIG 9—Case 3. Photomicrograph showing cellular infiltration of the musculature of the jejunum (High power).

FIG 10

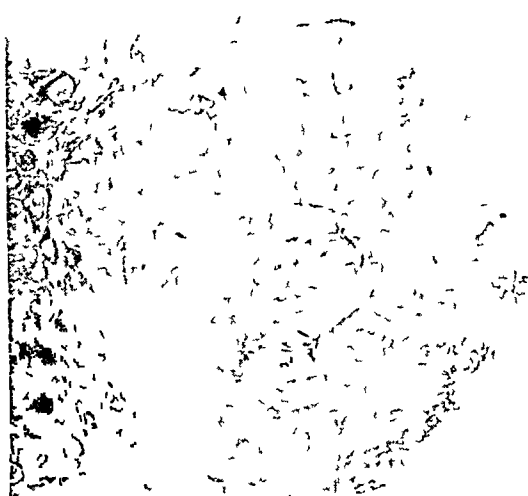


FIG 11

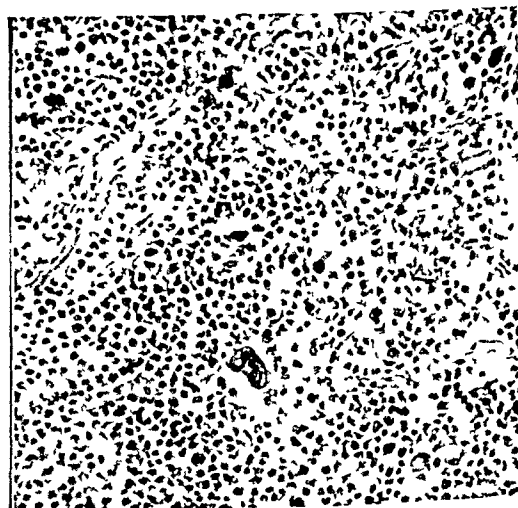


FIG 10—Case 3. Photomicrograph showing a mesenteric lymph node completely replaced on one side by lymphosarcomatous tissue. The uninvolved portion shows very large follicles (Low power).

FIG 11—Case 4. Photomicrograph of primary lymphosarcoma of the ileum (Low power).

The mucosal surface of the tumor was intact except for an ulcerated area 4 Mm in diameter at its mesenteric border. Microscopic examination of the jejunal and metastatic mesenteric tumors revealed closely arranged large round cells supported by a scant fibrous reticulum. Tissue eosinophile leukocytes were abundant in the primary tumor, but were scant in the mesenteric lymph nodes. Mitotic figures were not seen in the former location, but were present in the metastatic areas (Figs 8, 9 and 10). A diagnosis of lymphosarcoma was made.

Comment—This small constricting lymphosarcoma resembled grossly the most common type of primary malignancy of the small intestine, par-

ticularly of the proximal small intestine, namely, an annular carcinoma. It is noteworthy that postoperative survival and good health resulted for six years, even though there existed metastatic mesenteric nodules and direct extension of the tumor to the descending colon.

Case 4—S. H., male, age 64, was seen October 28, 1935, complaining of symptoms of cardiac failure which had been present four months. For one year the patient had been aware of the presence of an abdominal mass which, to his knowledge, had caused no trouble with the possible exception of a period of repeated vomiting which began six weeks before and stopped abruptly and completely two weeks later. The bowels had always been regular and free from gross evidence of blood. Except for heart sounds of poor quality and some moist râles in the bases of both lungs, the positive physical findings were limited to the abdomen and both lower extremities—an enormous, hard, nodular, immovable mass, which was only slightly tender, occupied all of the right side of the abdomen and the upper half of its left side. There was marked

FIG 12

FIG 13

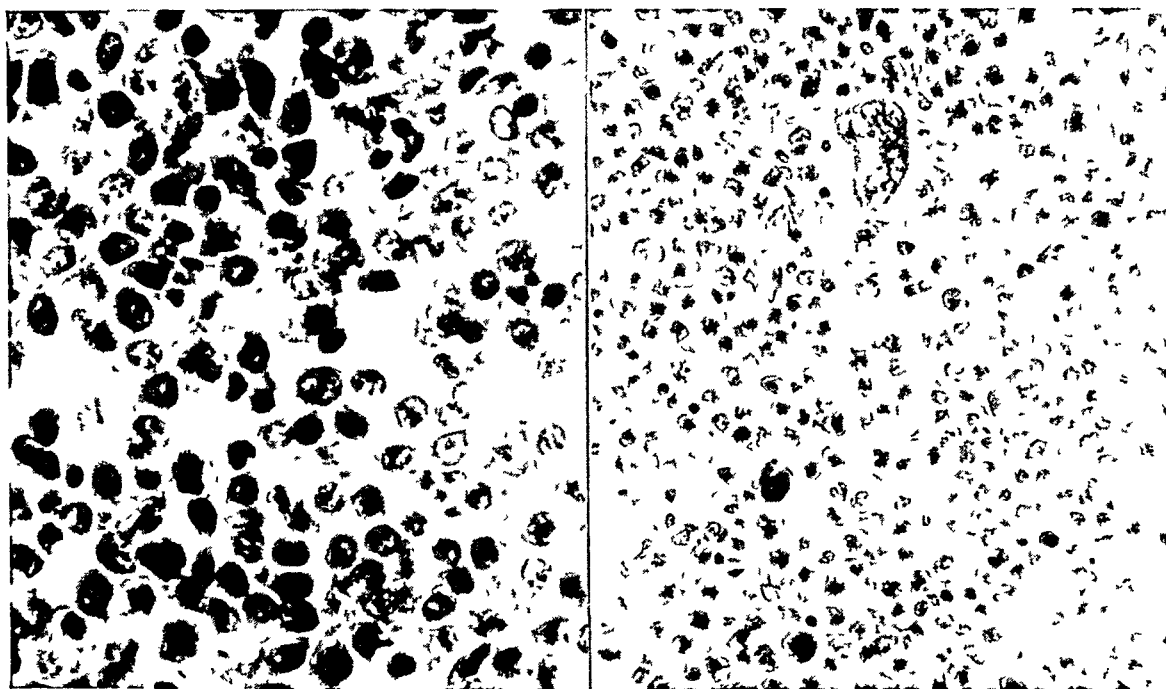


FIG 12—Case 4. Photomicrograph of a field which shows tumor cells which are typical of lymphosarcoma. (High power.)

FIG 13—Case 4. Photomicrograph of a field which shows tumor cells suggestive of Hodgkin's disease of the ileum. (High power.)

edema of the lower abdominal wall and both lower extremities. The blood Wassermann was negative, hemoglobin, 80 per cent, erythrocytes, 4,370,000, leukocytes, 2,325 to 4,850, and just before death, 850, seven differential counts gave the following percentage values: Polynuclears, 23 to 40, large lymphocytes, 27 to 43, monocytes, 3 to 11, eosinophiles, 6 to 19, and basophiles, 2 to 8. Four stool examinations gave one positive guaiac test. Roentgenologic studies after a barium meal showed no evidence of intrinsic involvement of the gastro-intestinal tract. A diagnosis was made of probable retroperitoneal sarcoma, and roentgenotherapy started. Death occurred from cardiac failure three days later.

Autopsy—There was found in the terminal ileum a chronic irreducible intussusception extending 2 cm into the lumen of the distal segment. The lumen of this intussuscepted bowel contained a firm nodule about 3 cm in diameter and at the distal end an irregular, polypoid nodular mass 5 cm wide, 2.5 cm long, and 2 cm thick. In the adjacent mesentery was found a mass 7 cm in diameter. *Microscopic examination* of the tumor revealed closely packed masses of large round or cuboidal cells with occasional

mitotic figures. The cells were supported by a scant fibrous stroma. There were occasional giant cells (Figs 11, 12 and 13). *Pathologic Diagnosis* Primary lymphosarcoma of the ileum with metastasis to the mesentery.

Comments—This case belongs to the group of primary malignancies of the jejunum-ileum which reveals no demonstrable clinical or roentgenologic evidence of intrinsic bowel pathology, and therefore presents insurmountable handicaps in clinical diagnosis. It is noteworthy, too, that histologic examination of this tumor reveals some fields which are typical of lymphosarcoma and others which are typical of Hodgkin's disease of the small intestine. This is, therefore, a lymphoid tumor of a borderline type, in which there is blending of two histologically different tumors.

CONCLUSIONS

- (1) Carcinoma and sarcoma of the jejunum-ileum are nearly equal in incidence, while malignant carcinoid accounts for 65 per cent.
- (2) Two-thirds of the primary neoplasms appear in the extremities and one-third in the intervening portions of the jejunum-ileal segment.
- (3) Eighty to 90 per cent of carcinomata and malignant carcinoids and at least 50 per cent of sarcomata produce mechanical obstruction of the bowel.
- (4) Infrequently, there are neither localizing symptoms nor positive roentgenologic findings of localized intestinal involvement.
- (5) Nonobstructive cases present almost insurmountable diagnostic difficulties.
- (6) Occult blood in the stool is inconstant and frequently of no material value in differential diagnosis.
- (7) Positive roentgenologic findings of localized intestinal involvement are essential for a diagnosis of small bowel neoplasm.
- (8) A clinical diagnosis of jejunum-ileal neoplasm is made correctly in approximately one-sixth of the cases.
- (9) A positive clinical and roentgenologic diagnosis of malignancy is seldom made and rarely warranted by the findings.
- (10) Approximately two-thirds of the cases are operable.
- (11) The operative mortality is 30 per cent and five year survival less than 10 per cent.

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SURGICAL ASPECTS OF LESIONS OF MECKEL'S DIVERTICULUM

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IN SPITE of the relative infrequency of the occurrence of acute intra-abdominal conditions as a result of some disease of a persistent Meckel's diverticulum, the literature on the subject has become quite extensive. This is perhaps true because the lesion is not common, the symptoms are dramatic and the embryologic malformation easily understood. While it is true most of the symptoms seen are the result of intestinal obstruction or peritonitis, the mechanism by which the obstruction or the peritonitis may be produced is quite varied. During the past few years we have had the opportunity of studying a representative series of these lesions and have been able to group them into certain well defined types. In view of the fact that most of the clinical reports that have been published stress only certain particular types, it has occurred to us that such a classification of the surgical aspects of this anomaly might be of value. The cases considered will be only those that have come to operation and will not include those instances in which a Meckel's diverticulum has been encountered accidentally, not being associated with the clinical syndrome for which the operative procedure was undertaken. Vitelline cysts, persistent omphalomesenteric ducts, malformations of the umbilicus and other anomalies due to omphalomesenteric remains will not be considered at this time. An exhaustive review of the literature, likewise, will not be undertaken as this has been adequately considered in several recent publications, especially those of Curd,¹ Christie,² Greenwald and Steiner,³ and Schullinger and Stout.⁴

Credit for the first mention of what subsequently was to be called Meckel's diverticulum is generally given to J H Lavater, in 1672 (quoted by Curd¹). It seems probable, however, that it was recognized even before then by Fabricius who advanced the conception that such diverticula arise from increased tension in the lumen of the intestine. Certainly Ruysch⁵ published an excellent illustration of the anomaly in 1701. At the turn of the eighteenth century, embryologists began to give considerable attention to the origin of the intestinal tract. This was crystallized by the appearance of Oken's and Kieser's^{5a} treatise in which they demonstrated the part played by the yolk sac. In their opinion, however, the yolk stalk persisted as the vermiform appendix. It was Meckel⁶ who showed the fallacy of this conception and

proved that whenever a persistence of the yolk stalk occurred it was always found in the lower part of the ileum. His findings have been summarized by F. T. Lewis⁷ as follows: "An out-pocketing of the human small intestine, usually about an inch in length but sometimes several times as long, had frequently been observed. It was generally found opposite the mesenteric attachment, about three feet from the beginning of the large intestine. Sometimes it was turned toward the mesentery. Its walls included all of the layers that went into the formation of the intestinal tube, with which its lumen was in free communication. He saw the diverticulum several times in children at birth, once in an embryo of six months and twice at three months. Since it is a congenital structure, essentially constant in position, Meckel sought to explain it through the normal development of the intestinal tract, and concluded as follows: 'Even into the third month of embryonic life a small elevation remains in the lower part of the small intestine as a trace of the former connection (with the yolk sac), and if this is retained beyond this time it appears as a blind appendage.'"

During the succeeding years numerous clinical reports appeared dealing with various intra-abdominal lesions produced by a persistent Meckel's diverticulum. Most of these dealt with various types of intestinal obstruction and while several instances of perforation and peritonitis had been reported, Fitz,⁸ in the first adequate review found in the American literature, states that after an experience of 13 years in the autopsy room at the Massachusetts General Hospital, he had never seen a single instance of adhesive peritonitis in connection with a diverticulum. It is of historic interest that in this same article Fitz states that "In the region where these congenital causes are most frequently met with, an occasional cause of intestinal strangulation, *viz.*, the vermiform appendage, is also found." This was two years before the appearance of his epoch-making publication on perforating ulcers of the vermiform appendix. In the light of present day knowledge it seems remarkable that such complete and accurate studies could have been made on the pathology of Meckel's diverticulum before the recognition of the much more frequent disease of acute appendicitis.

The incidence of Meckel's diverticulum is between 1 and 2 per cent according to the majority of statistical reports. The exact location of the diverticulum will depend upon the age of the individual and will likewise vary to a certain extent in different individuals of the same age. The site is apparently dependent upon the amount of growth taking place in that portion of the intestine proximal to the insertion of the stalk. In infants where complete growth has not occurred it may be found only a few inches from the ileocecal valve, while in adults it may be seen as far as three feet away. In the vast majority of instances the presence of a diverticulum produces no untoward symptoms. The diameter of the lumen closely approaches that of the ileum and the results of retention and obstruction are therefore uncommon.

The present study consists of observations made on 19 cases. These have been quite varied in their symptomatology and pathologic picture, yet can be grouped roughly into four clinical types:

(1) Catarrhal inflammation with or without associated regional complications

(2) Intestinal obstruction

(3) Gangrene of Meckel's diverticulum

(4) Peptic ulcer due to the presence of ectopic gastric tissue

(1) *Catarrhal Inflammation* with or without associated regional complications. While in this group we had only four cases, catarrhal inflammation of Meckel's diverticulum undoubtedly represents the most frequent type of in-

FIG 1

FIG 2



FIG 1—Photomicrograph of uncomplicated histologic picture of Meckel's diverticulum. Note the normal ileal mucosa (low power).

FIG 2—Photomicrograph of catarrhal inflammation of Meckel's diverticulum. The glands are distorted due to edema and exfoliation of the cells. There is infiltration of monocytes and polymorphonuclear leukocytes. The picture is one of nonspecific catarrhal enteritis limited to the diverticulum (low power).

flammation. Proof for this statement can be found in the numerous instances in which a Meckel's diverticulum is accidentally encountered giving anatomic evidence of a previous, old inflammatory process. This may present itself in the form of an organized peritoneal exudate causing adhesions between the diverticulum and the ileum at its base or between neighboring loops of intestine. Such adhesions may be the cause of intestinal obstruction, as will be discussed later.

Usually such an inflammatory process does not produce symptoms characteristic enough to result in its recognition. In one of our patients in which such an acute process was present (Fig 2) the symptoms were those of acute appendicitis without the localized tenderness and rigidity generally seen in this condition. At operation the diverticulum was edematous and injected and

was surrounded by omentum resembling the picture seen in the nonobstructive type of acute appendicitis

It is quite possible that a diffuse enteritis may remain localized in the diverticulum longer than in the rest of the small intestine due to poorer drainage. Because of the difficulty in diagnosis the symptomatology is still poorly understood. We have encountered one case in which such a process seemed to be instrumental in the production of a regional ileitis. When Crohn⁹ and his associates first isolated this specific clinical syndrome from other types of intestinal granulomata they described in detail a definite pathologic picture but stated that as yet the etiology was not understood. Since then various explanations have been offered, but so far all efforts to explain it on the basis of a specific type of infection have failed. Bockus and Lee¹⁰ have stated that "It is not unreasonable to postulate that any primary inflammatory mucosal disease in the terminal ileum might in the end resemble the entity under discussion." More recently Reichert and Mathes¹¹ have shown that an identical pathologic picture can be produced in an animal by the experimental production of intestinal lymphedema and thus add further evidence to the conception that a localized inflammatory process in the terminal ileum may through the presence of a chronic lymphangitis eventually produce such a picture.

This patient (Case 2) complained of intestinal cramps and constipation of about two years' duration. The findings at operation were characteristic of so-called "regional ileitis," beginning in the distal ileum just proximal to a Meckel's diverticulum and ending abruptly at the cecum. The wall of the diverticulum was in keeping with that of the remainder of the distal ileum. The mucosa was edematous and slightly hyperplastic. In several areas there were large accumulations of lymphoid material in the mucosa tending to displace the epithelium. The submucosa was markedly thickened due to edema as was the muscularis. There was a moderate amount of growing fibroblastic proliferation around the serosa (Fig. 3).

It is quite possible that the presence of the Meckel's diverticulum in this patient had nothing to do with the etiology of the process. The presence of a localized area of chronic enteritis in such a diverticulum, however, must be considered seriously as a causative factor.

Occasionally a patient is seen with the clinical picture of peritonitis which at operation is found to be due to a perforation of a localized ulcer in a Meckel's diverticulum. Careful examination of the tissue will show no evidence of ectopic gastric mucosa or pancreatic tissue. The cause of such a perforation may be a nonspecific, necrotizing type of inflammation or pressure necrosis from an impacted fecalith. Quite often, however, it is impossible to demonstrate the latter. We have had two such instances (Cases 3 and 4). In one of these the perforation was slow and at operation a well walled-off abscess was found. In the other the symptoms were fulminant and resembled to a

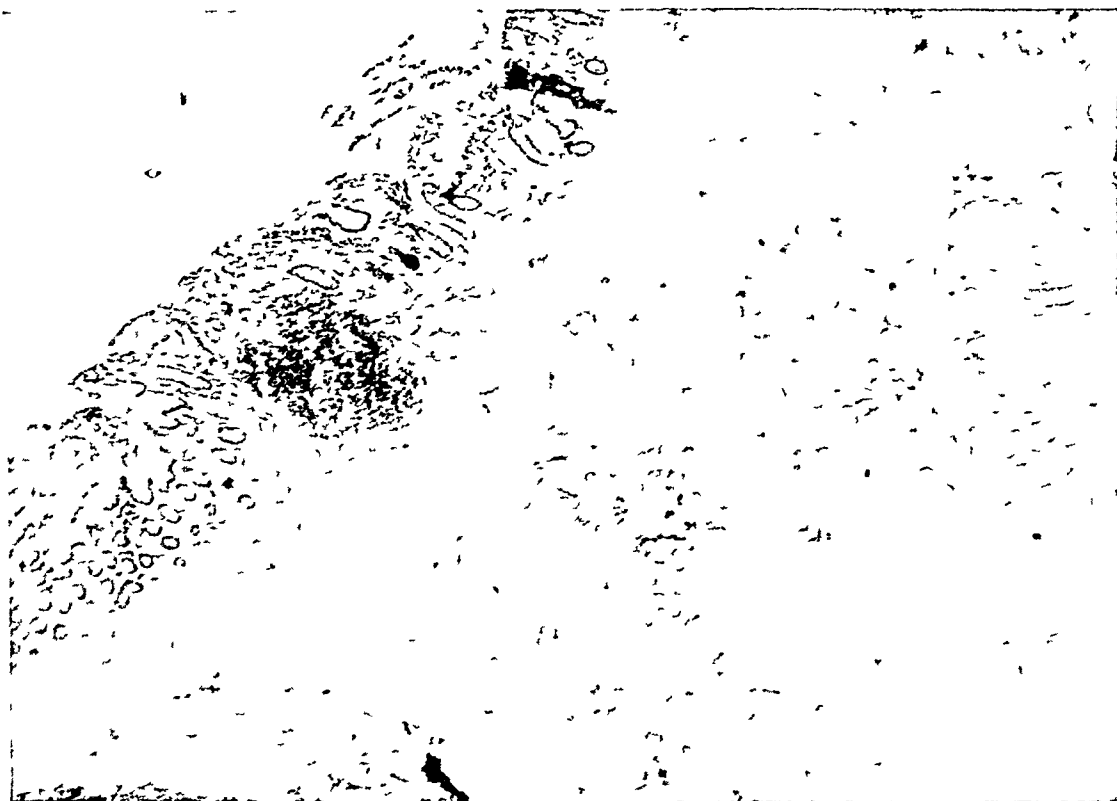


FIG 3—Photomicrograph of the wall of the diverticulum involved in the regional ileitis. Note the massive edema of the submucosa with the presence of a lymphoid nodule immediately beneath the epithelium. The epithelium is desquamating into the lumen in several places. The muscularis stains poorly and is likewise edematous.



FIG 4—Photomicrograph of the edge of a nonspecific ulcer which had perforated causing localized peritonitis. There is no evidence of ectopic gastrointestinal epithelium seen. The picture is that of a localized area of necrosis.

considerable degree the picture of a perforated duodenal ulcer (Fig 4) In neither case was it possible to explain adequately the cause of the perforation

(2) *Intestinal Obstruction*—We have observed five instances in which some type of intestinal obstruction resulted from the presence of a Meckel's diverticulum. As has been stated, early reports of lesions of Meckel's diverticulum were for the most part concerned with intestinal obstruction. Indeed, Meckel himself called attention to the fact that the persistent remnant of the yolk stalk or the omphalomesenteric vessels extending down to the tip of the diverticulum could easily act as a band causing such an obstruction. This is probably the mechanism in what is perhaps the first reported case of intestinal obstruction due to this cause, namely, that of Van Doeveren as described by Sandifort,¹² in 1793. These bands do not necessarily always lead from the tip of the diverticulum to the umbilicus but may have many bizarre attachments, the mesentery being perhaps the most common. The defect produced is generally that of a tunnel through which loops of bowel may migrate and subsequently become strangulated. At other times a diverticulum may become twisted upon itself and in so doing obstruct an adjacent loop of bowel. A number of these methods have been described by Cullen¹³ with accompanying illustrations. That the tip of a diverticulum may become adherent to a distant point as the result of a peritonitis secondary to diverticulitis and serve as a cause of obstruction is well illustrated in Case 3. Earlier writers, especially Titz, either doubted the occurrence of such a condition or else thought it extremely rare. We have observed it several times.

A Meckel's diverticulum acting as the starting point for an intussusception of the ileum, while observed before, is still rare enough to warrant a detailed description.

Case Report—M. B., white, female, age 11, entered the St. Louis Children's Hospital, December 10, 1935, with the complaint of abdominal pain and vomiting for six days. Her past history was uneventful with the exception of a slight attack of nausea and headache a year previously, for which there had been no explanation. At noon, six days before her admission to the hospital, she experienced sharp, shooting pains in the abdomen localized about the umbilicus. This had been preceded shortly before by diarrhea. During the afternoon she began to vomit and continued to do so at intervals until her admission. She had been given repeated enemata with no results after the first one with the exception of the presence of blood first noted two days before admission. Distention had been present for 24 hours.

Physical Examination—She appeared acutely ill, but was alert and cooperative, the eyes appeared sunken and the skin was dry and gray. There was a slight nasal discharge. The lips were dry and cracked. The pharynx was injected. The chest was normal, pulse 120. The abdomen was distended and tender throughout, the right side more so than the left. There was no rigidity. Rectal examination revealed no masses but definite peritoneal tenderness. An enema revealed a few flecks of blood. Temperature, 38° C. White blood count, 11,000.

After parenteral fluids had been given, a celiotomy was performed by Dr. W. H. Cole. A large quantity of straw-colored fluid escaped from the abdomen. The small intestine was greatly dilated and filled with fluid. An obstruction was located about six inches above the ileocecal valve. It was obvious that an intussusception had oc-

curred at this point and that the ileum for a distance of about six inches was filled with intussuscepted ileum. Reduction was impossible due to gangrene. Accordingly the mesentery was divided and a resection performed, the ends of the bowel being brought out in double-barrel fashion. A clamp was placed on the lower loop and a catheter in the upper loop. The wound was closed and a blood transfusion given. With the exception of a moderate amount of infection around the ileostomy wound, which readily cleared up, convalescence was uneventful. The ileostomy was closed February 13, 1936. The distal loop was too short for an end-to-end anastomosis and accordingly was closed and the proximal loop anastomosed to the cecum end-to-side. Convalescence was uneventful and the patient was discharged March 12, 1936.

Pathologic Examination—Gross The material consisted of a piece of the terminal ileum. Because of the gangrene present it was impossible to reduce the intussusception and still keep the gut intact. By splitting the wall of the intestine, however, it was possible to see each of the layers and by doing this demonstrate that the intussusception contained three layers of intestine in the center of which was a Meckel's diverticulum, the tip of which was quite swollen, there being considerable necrosis of the entire diverticulum. It is apparent from the appearance of this specimen that the diverticulum was the cause of the intussusception.

Microscopic—A section taken through the diverticulum showed tissue difficult to demonstrate because of necrosis. The mucosa was completely destroyed as was the submucosa, only a small piece of the longitudinal muscle remaining. There was infiltration by pus cells. The picture was that of intestinal strangulation.

(3) *Gangrene of Meckel's Diverticulum*—The diverticulum generally projects from the convex or antimesenteric surface of the ileum. It may or may not have a mesentery. Where none exists the diverticulum is often found in close approximation to the intestine, receiving its blood supply from the intestinal wall. Where a mesentery exists remnants of the omphalomesenteric vessels may at times be found. As a rule the blood supply comes from the mesentery of the small intestine, passes over the ileum and spreads out in a capillary network over the wall of the diverticulum. It is quite possible at times that the blood supply may be insufficient for excessive demands. In such instances the pathologic sequence is comparable to the changes taking place in acute obstruction of the vermiform appendix. The lumen of the diverticulum, including its orifice, is generally large, often approaching the diameter of the ileum from which it arises. For this reason obstructive phenomena are not as common as would be present in a structure where retention of fecal material and the formation of fecaliths is more frequent. We do feel, however, that a localized obstruction to the lumen of the diverticulum can occur with distention and secondary vascular changes with gangrene. We have observed one instance in which the process had become gangrenous and had separated from the ileum at its base just as is the case in acute appendicular obstruction.

Case Report—J. B., male, age 26, was admitted to the St. Louis City Hospital, August 21, 1935, with the complaint of severe, acute abdominal pains localized over the lower abdomen, which had begun suddenly two hours before admission. There had been no previous attacks. The pain had been followed shortly by nausea and vomiting. Further questioning revealed that the patient had eaten a dinner of corn "roasting ears," and about five hours later the pain began.

Physical Examination revealed a well developed and well nourished young man, moaning with pain and rolling about in bed. There was a tendency for him to keep both knees flexed and hold his hands over the abdomen. In general the objective findings were negative except for those in the abdomen. This was not distended and moved with respirations. There was considerable tenderness just below and to the right of the umbilicus which was not associated with either rigidity or muscle guard. There was rebound tenderness across the entire lower abdomen. No masses were palpable. Rectal examination revealed tenderness high on the right side but was otherwise negative. The temperature, pulse and respirations were normal, as were the blood and urine studies, except for a leukocytosis of 15,000.

Operation—The abdomen was opened through a lower right paramedian incision. There was an escape of about 200 cc of clear fluid. The entire terminal ileum and cecum were distended with whole grains of corn. The appendix was slightly injected, long and extended toward the midline. While obviously not the cause of the symptoms, it was removed and the stump inverted. Further exploration showed a cyanotic Meckel's diverticulum, which was markedly distended with corn. The gross appearance was that of an early intestinal obstruction. The diverticulum was removed and the opening closed and inverted. Convalescence was uneventful.

Pathologic Examination—The mucosa of the diverticulum resembled that of the ileum. No ectopic tissue was seen. The outstanding feature was the presence of extensive venous congestion and submucosal hemorrhage, such as is seen in early intestinal obstruction. Upon section, the lumen of the appendix contained a few half grams of corn. The vessels were slightly injected but microscopically the wall showed no evidence of necrosis or cellular infiltration.

We have observed evidence of strangulation of the diverticulum on four occasions. In one of these the necrosis was so complete that no explanation of the origin was possible.

(4) *Peptic Ulcer of Meckel's Diverticulum*—Ulcer of Meckel's diverticulum associated with the presence of ectopic gastric mucosa has been noted only relatively recently. Such glandular tissue was first described around the umbilicus by Tillmanns,¹⁴ in 1882. This was a pedunculated polyp that extended out from the umbilicus of a boy, age 13. The tumor secreted a fluid that would digest fibrin in an acid medium. It was removed and microscopic examination revealed the presence of tissue identical to that of the stomach mucosa. Following this report, others noting similar phenomena were published. While perforating ulcers of the base of the diverticulum were also being reported, exact identification of the presence of gastric mucosa in a diverticulum was not apparent until Salzer,¹⁵ in 1904, described the prolapse of a Meckel's diverticulum, containing gastric mucosa, through the umbilicus. The association between the gastric mucosa and the perforating ulcer was made by Schaetz,¹⁶ in 1925, who showed the marked similarity between peptic ulcers of the stomach and duodenum and those penetrating ulcers often seen associated with a Meckel's diverticulum. He showed the presence of gastric epithelium in five out of 30 patients, and explained the frequent occurrence of intestinal hemorrhage before the perforation as being due to such ulceration. In the few years since then numerous other reports have followed until a very well defined clinical and pathologic picture is now recognized. The circumscribed punched out ulcer is generally seen at the junction of the gastric

mucosa with that of the ileum, although this is not always the case (Fig 5) Not only has the presence of such an ulcer been explained as due to the pouring of acid gastric secretion over the ileal mucosa, but also has been used as evidence of the peptic genesis of gastric and duodenal ulcers by Lindau and Wulff¹⁷ Diagstedt,¹⁸ in discussing this pathogenesis of diverticular ulcers, draws attention to the fact that it likewise offers further proof of the humoral mechanism governing gastric secretion as maintained by Ivy and Farrell¹⁹

The outstanding single symptom that distinguishes this lesion is bleeding from the rectum In the vast majority of cases it has occurred in children It can be distinguished from the hemorrhage in those relatively rare cases of bleeding peptic ulcers of the duodenum in children by the fact that the blood is generally more profuse and is also red It is likewise not mixed with the



FIG 5—Photograph of the gross specimen showing a perforating peptic ulcer of Meckel's diverticulum The ulceration can be seen at the junction of gastric and ileal mucous membrane

stool, as is the case in duodenal ulcers and intussusception Such hemorrhage is occasionally seen in patients with rectal polyps but such a lesion can be ruled out by proctoscopic examination Pain may or may not be present Unless the ulcer is beginning to perforate it is not unusual to find no associated abdominal findings These hemorrhages may be recurrent and appear at intervals, months before perforation, and may result in a severe secondary anemia In 66 collected cases of peptic ulcers of Meckel's diverticulum, Schullinger and Stout found that hemorrhage had been mentioned as being present in 51, or 75 per cent So characteristic is this hemorrhage that Abt and Strauss²⁰ have operated upon three such patients before perforation, and removed a diverticulum in each case that contained an ulcer associated with ectopic gastric mucosa

When perforation occurs, the signs and symptoms are those associated with

any sudden, massive soiling of the peritoneal cavity namely, pain, nausea, vomiting and abdominal rigidity and tenderness. Certainly the presence of such an acute abdominal catastrophe with a history of rectal hemorrhages should usually make the diagnosis apparent.

Case Report—L O, white, male, age 10, was admitted to the St. Louis Children's Hospital, February 12, 1934, with the complaint of blood in the stools. At the age of four, preceding an attack of measles, the child had fainted for no apparent cause. Since then he had had four such attacks, the last the day before admission. He would become unconscious, fall to the floor with arms and legs drawn up and after a few minutes would appear normal again. He had occasional attacks of nose bleed. The day before admission the boy passed a large quantity of dark blood in his stool and shortly afterward fainted. A similar stool was passed on the day of admission but was not associated with fainting. During the past six or eight months he had complained of vague pains about the navel that came and went and which were not associated with nausea and vomiting.

Physical Examination was negative with the exception of several bruises on his legs, enlarged tonsils and a moderate anemia. Erythrocytes, 3,440,000, hemoglobin, 70 per cent. Proctoscopic examination showed no cause for the bleeding. A gastrointestinal roentgenologic examination revealed a pathologic appendix, due to the presence of fecaliths. Platelet count, clotting and bleeding time, normal. There was no further evidence of blood in the stools, other than the mother's statement, and after observation the child was discharged February 19, 1934.

He was readmitted to the hospital, March 3, 1934, with the history that he had been weak and listless since his discharge. The day before his second admission bright red blood had been noted in two stools. He had fainted twice. There had been no pain, nausea, or vomiting. On the day of admission he had passed bright blood in two stools and dark blood in the last. He had fainted on two occasions. At this time the red blood count was 2,000,000 and the hemoglobin 60 per cent, white blood count, 17,000. He was given a blood transfusion. Again there was no evidence of bleeding from the rectum upon examination of the stool and further proctoscopic examination was negative. On March 10, 1934, he complained of pain in the right lower quadrant which was associated with tenderness and muscle guard, which subsided quickly. An enema given at this time showed no blood in the return.

Operation—(Dr. Peter Heinbecker) The abdomen was opened through a right rectus incision, and a moderate amount of thin, turbid, odorless yellow fluid escaped. About 18 inches from the ileocecal junction a Meckel's diverticulum, about two inches long, was found with a perforation at its base at the junction with the ileum. The tip was buried in the mesentery, and there was a fresh deposit of fibrin on the bowel in this region. The diverticulum was excised, and because of the edema of the bowel wall, a catheter inserted. The wound was closed with no further drainage. The post-operative course was uneventful. The ileostomy tube was removed several days later and the patient discharged two weeks after the operation.

Microscopic Examination of the diverticulum showed characteristic gastric mucosa except at the base where there was a perforating ulcer containing a considerable amount of old fibrous tissue, indicating that it had probably been present for some time.

Discussion—Table I shows some of the features of the 20 cases of lesions associated with a Meckel's diverticulum that have produced acute abdominal conditions. Such a series is too small to warrant any statistical analysis because of the obvious percentage of error that would arise as a result of coincidence. Certain features, however, are in accord with other reports. Males predominate markedly. Almost one-half of the cases are in children, age 10 or

MECKEL'S DIVERTICULUM

TABLE I

Name	Age	Sex	Group	Gross Appearance	Microscopic Appearance	Result
M L	14	F	1	Edema and cyanosis of diverticulum	Catarrhal inflammation with erosion of epithelium	Recovery
L G	23	M	1	Regional ileitis extending from diverticulum to cecum	Lymphoid invasion Edema of entire wall	Recovery
C S	54	M	1	Perforated ulcer with associated peritonitis	Perforating ulcer of diverticulum with no associated ectopic tissue	Death
B L	18	F	1	Perforating ulcer of tip of diverticulum with adhesions to intestine	Perforating ulcer of diverticulum with no associated ectopic tissue	Recovery
M B	11	F	2	Intussusception of lower ileum beginning with diverticulum	Necrosis	Recovery
A H	4	M	2	Obstruction at site of previous removal of Meckel's diverticulum		Recovery
H C	6 mos	M	2 and 3	Intestinal obstruction due to persistent omphalomesenteric vessels with gangrene of diverticulum	Gangrene of diverticulum	Recovery
S L	50	F	3	Beginning strangulation of diverticulum in ventral hernia	Early strangulation	Recovery
L K	8	F	3	Gangrene of diverticulum with perforation and abscess formation	Necrosis	Recovery
B C	11 mos	F	3	Necrosis of diverticulum with peritonitis	Necrosis	?
J B	26	M	3	Distention of diverticulum with corn, with edema and cyanosis	Early gangrene of entire wall of diverticulum	Recovery
W R	2½ mos	M	4	No history of rectal bleeding Perforating ulcer at base of diverticulum with peritonitis	Ectopic gastric and pancreatic tissue	Death
K W	6 mos	M	4	History of rectal bleeding Perforating ulcer at base of diverticulum with peritonitis	Ectopic gastric mucosa	Recovery

TABLE 1 (Continued)

Name	Age	Sex	Group	Gross Appearance	Microscopic Appearance	Result
A H	6	F	4	No history of rectal bleeding Perforating ulcer at middle of diverticulum at edge of gastric mucosa	Ectopic gastric mucosa	Recovery
L O	10	M	4	History of rectal bleeding Perforated peptic ulcer at base of diverticulum	Ectopic gastric mucosa	Recovery
S F	2 days	F	4?	Massive rectal hemorrhoid shortly after birth with diverticulum and intestine distally filled with blood	?	Death
W B	11	M	4	No history of rectal bleeding Perforated ulcer at base of diverticulum with peritonitis	Ectopic gastric mucosa	Recovery
E H	14	M	4	Rectal bleeding Acutely inflamed diverticulum No gross ulcer	Ectopic gastric mucosa	Recovery
J E	19	M	4	No history of rectal bleeding Acutely inflamed diverticulum with no area of perforation No gross ulcer	Ectopic gastric and duodenal mucosa	Recovery

under. Approximately one-half of the cases are associated with obstruction of the diverticulum itself or obstruction of adjacent loops of intestine. This is interesting in view of the fact that Griffith,²¹ in describing various types of diverticulitis quotes Halsted²² as stating that in a series of 991 cases of intestinal obstruction he found that 6 per cent were due to the presence of a Meckel's diverticulum.

Two of our cases illustrate the apparent ease with which the blood supply to a diverticulum may become jeopardized. In one (H C) persistent omphalomesenteric vessels extended in a cord-like fashion from the end of a diverticulum to become attached in the mesentery of an adjacent loop of ileum. A loop of bowel slipping under this cord had become completely obstructed. The blood supply to this bowel, however, was still adequate while that of the diverticulum had been completely cut off and gangrene had supervened. Apparently the blood supply to the diverticulum could not stand as much interference as could that of the normal gut. In the other case (S L), that of an incarcerated ventral hernia in the sac of which ileum was present containing a Meckel's diverticulum, there was evidence of early strangulation of the diverticulum while the remainder of the bowel showed no evidence of circulatory change.

In view of the relative infrequency of disease of Meckel's diverticulum and

the apparent frequency of the occurrence of the structure, obviously the vast majority produce no symptoms. The lumen is large and the musculature is well developed, so that emptying apparently occurs quite satisfactorily. For this reason judgment must be used as to whether or not the diverticulum should be removed when it is encountered accidentally while operating for some other condition. Case A. H. illustrates this fact. This four year old boy had been operated upon for acute appendicitis a year previously. A diverticulum was present in the operative field and although the appendix had perforated, the diverticulum was removed at the same time. He developed signs of acute intestinal obstruction a year later and at operation the obstruction was found to be due to a band of adhesion which had its origin at the site of the diverticulum.

In this series there were seven cases of ulceration due to the presence of ectopic gastric mucosa (Fig. 6). In three of these there was no history of

FIG. 6

FIG. 7



FIG. 6 —Photomicrograph showing normal gastric mucosa found adjacent to the ulcer seen in Figure 5.

FIG. 7 —Photomicrograph showing both gastric and duodenal glands. While this patient gave a history of both recurrent rectal hemorrhage and pain, no evidence of ulceration was seen in the gross specimen. The mucosa was hypertrophic.

hemorrhage. All but one had perforated at the time of operation. Six recovered. It is interesting that many of these ulcers occur relatively late in childhood. If the presence of an acid secretion alone is sufficient to produce ulceration, one would expect that this would be predominantly a disease of infancy. It is quite possible that the presence of local trauma also plays a part.

In one of our cases duodenal mucosa was also present along with the gastric glands (Fig. 7). The hyperplasia of this tissue was quite marked, almost filling the lumen and giving an adenomatous appearance. Although the patient gave a history of intestinal hemorrhages for several years we were unable to demonstrate the point of ulceration. The appearance bore a striking resemblance to the case reported by Schullinger and Stout. In their quite complete review of the literature they were unable to find another reported example of gastric and duodenal gland adenoma.

Another of our cases presented a nodule of pancreatic tissue in the wall of

the diverticulum along with associated gastric mucosa (Figs 8 and 9) The pancreatic tissue was apparently normal in every respect and had not seemingly entered into the ulcerative process Islets were present, as one would expect, due to the common origin of islet and acinar tissue The presence of aberrant pancreatic tissue in a Meckel's diverticulum has been recognized for many years,²³ yet its occurrence is extremely rare In a recent review of the subject Hunt and Bonesteel²⁴ were able to find only 13 recorded cases To this they have added one of their own The above case, therefore, would make the total 15

Adequate explanation of the presence of heterotopic gastric mucosa in the diverticulum, as is true with other ectopic tissue, is not easily obtained Detachment of the vitelline duct has generally occurred by the time the 7 Mm stage is reached in the embryo, although this is not always constant as its presence has been noted in embryos of a later stage (12.4 Mm and 13.6 Mm)

FIG 8



FIG 9

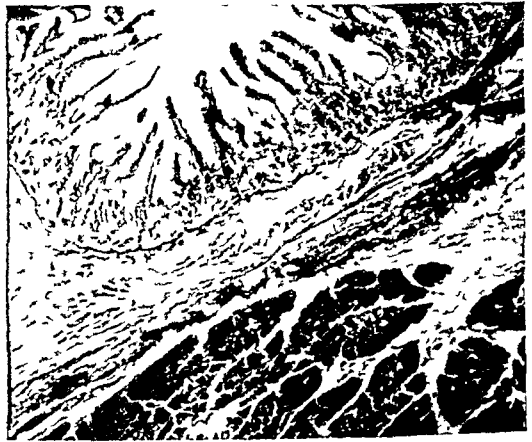


FIG 8—Photomicrograph of a longitudinal section through a Meckel's diverticulum showing gastric glands in the mucosa associated with a nodule of pancreatic tissue attached to the wall This patient had a perforating ulcer at the junction of the diverticulum and ileum (low power)

FIG 9—More highly magnified photomicrograph of an area of Figure 8 showing the close proximity of the pancreatic tissue to the wall of the gut

It would seem, therefore, that by the time this age is reached in the embryo any persistent pouch from the vitelline duct would be already formed Certainly this occurs considerably earlier than the gastric glands become differentiated in the stomach As a general rule eosinophilic and parietal cells have not become differentiated from each other until the 120 Mm stage (Kerbel and Mall) The theory that this tissue arises from dislocated or misplaced gastric or other adventitious cells would, therefore, seem to be untenable The other conception that has been advanced is faulty differentiation by the primitive endoderm While this has been the preferred explanation of most observers the exact reason for this faulty differentiation has resulted in no unanimity of opinion At the present time it is not subject to experimental proof

Mammalian cellular differentiation is poorly understood in many of its aspects While in times past it has been simple to explain the presence of

ectopic tissue by assuming the dislocation of predetermined cells, adequate proof of either the dislocation or the predetermination has not been easy. The conception of an "organizer" substance as advanced by Spemann²⁵ has been developed considerably during the past decade and has much to offer in the explanation of such phenomena. While more of the earlier work²⁶ was concerned with symmetry and form, more recently much of it has had to do with functional cellular change and local organizer effects. Apparently this determinism is progressive. Various fields may influence each other. An example may be seen in the relationship between the buccal ectoderm and endoderm in tooth formation. Stroer²⁷ has recently shown that teeth are formed from the buccal ectoderm. However, this ectoderm is dependent upon the buccal endoderm that lies directly beneath it for its power. If this endoderm be removed the ectoderm develops into epidermis. Besides spatial effects on cellular differentiation, physical and chemical action may play no small part.

When this complex arrangement is considered, it does not appear remarkable that a persistent rudiment such as a Meckel's diverticulum should show the presence of other tissues of the gastro-intestinal tract than that of the ileum. The exact mechanism of the appearance of this tissue, however, will not be evident until detailed cellular differentiation in the mammalian gastro-intestinal tract is better understood.

CONCLUSIONS

(1) Nineteen cases of various aspects of acute abdominal lesions associated with Meckel's diverticulum are reported.

(2) These cases are divided into four distinct groups, each of which is discussed in detail.

(3) The mechanism of the occurrence of ectopic tissue in the wall of a Meckel's diverticulum is discussed briefly.

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TRAUMATIC RUPTURE OF THE BILE DUCTS

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RUPTURE of the bile ducts is an interesting and rare complication of traumatism of the right upper quadrant of the abdomen. Rudberg,¹ in 1921, reviewed the subject and collected 41 cases. Garriett,² in 1900, reported a case, and Walter Spencer,³ in 1898, also cited an instance. Since 1921, we have been able to find only six additional cases reported (Long,⁴ Anderson,⁵ Just,⁶ Leclerc,⁷ Wallace and Spiro,⁸ and Edington⁹). These six cases with the 41 collected, in 1921, by Rudberg, bring the total number of cases in the literature, to date, to 47.

Etiology—The cause of rupture of the bile ducts is practically always a crushing trauma to the right upper quadrant of the abdomen in the region of the costal margin. Why the hepatic or common bile duct should be torn without any associated laceration in the liver, as is the situation in most of the cases reported, is difficult to understand. The explanation that seems logical is that the force is applied in such a direction as to crush the ducts between the liver and the bodies of the vertebrae at that level. The absence of fractures of the ribs or of injury to any of the hollow viscera in the abdomen is difficult to explain. In the case herewith reported, the trauma consisted of the patient's being crushed between two automobiles, and this cause was also noted in the case reported by Long.

Clinical Findings—In most of the case histories reviewed, it has been noted that the patients were in rather profound shock at first, and complained of severe pain in the region of the liver. The shock was usually of rather short duration, and was recovered from within a few hours. At the end of from one to ten days, considerable increase in the size of the abdomen was noted, which in all cases was found to be due to fluid. Associated with this fluid accumulation in the abdomen, the patients developed increasing jaundice, clay-colored stools, bile in the urine, and in most instances a gradually rising temperature with a progressive toxemia. They usually appeared critically ill, and complained of profound exhaustion, which had rapidly increased in degree.

In our own case, we were somewhat confused by signs of consolidation at the base of the right lung, which developed 24 hours after the injury. Pneumonia has not been a frequent complication, and the diagnosis of rupture of the biliary ducts should readily be made if the cardinal signs of rapidly increasing fluid in the abdomen, jaundice and clay-colored stools are borne in mind. There can be no other intra-abdominal condition which can simulate these findings, but if a question of differential diagnosis does arise

paracentesis will yield large quantities of pure bile from the peritoneal cavity. Fortunately, the bile remains uninfected, and whereas all of the abdominal organs become deeply bile stained, the finding of a real suppurative peritonitis has so far not been reported.

Treatment—Exploratory celiotomy is, of course, primarily indicated, preferably through a right, upper rectus muscle-splitting incision. Upon opening the peritoneum, there is an escape of large quantities of pure bile from the peritoneal cavity, seven quarts being aspirated through the abdominal incision in our case.

Exploration of the right upper quadrant will show the tear if it is situated in the common or cystic ducts, but if in the hepatic duct, it frequently cannot be seen. The diagnosis in such a case may be made by the constant stream of bile which may be seen pouring down from the region of the hepatic duct, high up under the liver. In most of the cases operated upon, the primary treatment has usually been conservative, as the patients are usually profoundly ill and cannot withstand any extensive surgery. Simple drainage by means of a cigarette drain down to the site of the tear is to be recommended, without any attempt at suture repair, even in those cases where the tear is visible. Repair of a rupture of the hepatic duct is usually technically impossible due to its inaccessibility. Closure of the abdominal wound in layers, followed by adequate postoperative supportive measures, particularly the administration of large amounts of fluid, both by vein and hypodermoclysis, is indicated. If the patient has been operated upon before the toxemia has become too profound, recovery from the immediate condition usually ensues. There is a drainage of bile from the abdominal wound for a period varying from several weeks to several months. At the end of this time the tear in the bile duct usually heals spontaneously and the biliary fistula closes. A stenosis of the duct at the site of the tear may occur, which complication unfortunately occurred in our case. If the original tear and the subsequent stenosis are in the common duct, secondary operation with a cholecysto- or choledochoduodenostomy or a cholecysto- or choledochogastrostomy may be performed, but if the tear is situated high up in the hepatic duct, the relief of the ensuing jaundice due to the stenosis is a most difficult problem.

Case Report—F S, male, age 49, truckman by occupation, was admitted to the Fourth Surgical Division of Bellevue Hospital, July 30, 1931, with a history of having been crushed between two trucks shortly before admission. The trauma involved the right upper quadrant of the abdomen in the region of the costal margin. When first seen by the ambulance surgeon, the patient was in moderate shock, which had, however, subsided by the time he was admitted to the hospital, although considerable pain in the region of the right costal margin was complained of. He refused to stay in the hospital, and as immediate examination revealed no apparent serious injury, he was allowed to go home with the right side of the chest strapped with adhesive plaster. On August 1, 1931, two days later, the patient returned to the hospital, complaining that there had been a progressive increase in the pain in the right upper quadrant of the abdomen. He had developed a cough, vomited once, and his temperature was 101° F. He appeared acutely ill, was quite weak, and was in a profuse perspiration.

Physical Examination revealed a distended abdomen, with marked tenderness and rigidity in the right upper quadrant. Examination of the lungs disclosed dulness, bronchial breathing, and showers of fine crepitant rales at the right base. A diagnosis of right lower lobar pneumonia was made. The patient's temperature ranged between 101° and 104° F, pulse 100 to 130. The distention of the abdomen grew progressively more marked each day which was thought at first to be the result of a paralytic ileus, consequent to the pneumonia. On the fourth day it was noted that there was a large amount of fluid in the abdomen. At this time the patient also first began to become jaundiced, and bile was found in the urine. Twenty-four hours later, or seven days after the injury, the jaundice had become very marked, the stools were clay-colored, the abdominal distention had increased tremendously, and the urine showed large quantities of bile. There was persistent localized tenderness over the right upper quadrant of the abdomen, and the pneumonia in the right chest showed signs of resolution. Diagnosis of rupture of one of the bile ducts was made.

Operation—August 9, 1931. 11 days after the injury. The abdomen was opened through a right upper rectus incision and was found to contain an enormous amount of free bile. About five quarts were aspirated, and it was estimated that another two quarts were lost in spillage. All the abdominal contents were deeply bile-stained. Exploration showed no tear in the liver, gallbladder, cystic or common ducts. A constant stream of bile was seen to be seeping from the region of one of the hepatic ducts, but the actual tear in the duct could not be identified. In view of the patient's poor condition, further exploration was deemed inadvisable. A cigarette drain was inserted into Morrison's pouch, and the wound closed in layers.

Postoperative Course—Convalescence was somewhat stormy for the first few days. There was a profuse drainage of bile from the wound, which continued unabated for about ten days. The jaundice gradually disappeared, but the stools continued to be clay-colored. The bile gradually disappeared from the urine. On September 4, 1931, 27 days after the operation, the patient was discharged, with a small sinus still draining bile and with the stools still clay-colored, but with the other symptoms having disappeared. One month later the sinus had healed, the discharge of bile had ceased, and normal color had returned to the stools. In November, 1931, two months later, the patient was again admitted to the hospital with a history that during the preceding month, he had become gradually more and more jaundiced and that the stools had again become very light in color. Icteric index at this time was 35, the urine showed a large amount of bile. It was felt at this time that the patient's original injury had been a laceration of the common hepatic duct, that the laceration had spontaneously healed, and that, unfortunately, the scar tissue healing had contracted down with a resulting stenosis. The patient was kept under observation in the hospital for one month, during which time repeated biliary drainages would produce a temporary flow of bile into the duodenum but at no time did the jaundice entirely disappear. Further exploration of the abdomen was decided upon in an attempt to relieve the stenosis.

Second Operation—January 16, 1932. A right upper rectus incision was made, excising the original scar. The gallbladder, duodenum, stomach and transverse colon were found matted together by extremely firm, dense adhesions. These were separated by both blunt and sharp dissection with great difficulty. The common bile duct was finally exposed, and was followed upwards beyond its junction with the cystic duct, into the sulcus in the liver. Scar tissue could then be felt in the common hepatic duct, high up under the liver, but it was impossible to expose the stricture so that it could be seen. In view of its inaccessibility, and the fact that any reconstruction operation would not be feasible, it was decided that it would be unwise to proceed further. The wound was closed in layers with a cigarette drain left in, in case there was any oozing which might take place from the raw surfaces.

Postoperative Course—Five days postoperative, a duodenal fistula developed probably as a result of necrosis where a ligature had been applied to the anterior duodenal

wall to control bleeding from an adhesion. This condition proved to be quite stubborn, but ultimately healed after a period of five weeks' continuous suction of the fistulous tract. The jaundice spontaneously subsided, and it had entirely disappeared by April, 1932. As a result of the infection of the wound from the duodenal fistula, a ventral hernia developed, which was repaired in May, 1933.

Follow-Up—The patient has now been kept under observation for a period of over six years. Duodenal drainages are instituted once or twice a week, and if these are persisted in, the patient remains quite comfortable. There is always a residual jaundice which becomes intensified if the biliary drainages are allowed to lapse. Normal color is returned to the stools shortly after the second operation. The biliary drainages always produce a good quantity of golden-yellow bile, but no concentrated green bile is ever found.

About once every six months the patient has an attack of severe pain in the right upper quadrant of the abdomen, associated with a sudden increase in the intensity of the jaundice and a lightening in the color of the stools. There is usually a rise in temperature to 102° or 103° F. These attacks are relieved by hypodermics of morphine sulphate grains one-quarter, plus an icecap to the gallbladder region, followed shortly thereafter by duodenal drainage. One would assume that on these occasions the bile may become somewhat inspissated at the site of the stricture, causing a sudden complete obstruction with back pressure on the hepatic radicals in the liver. The attacks are always over within a day or two and do not recur with any great frequency.

Further exploration of the abdomen in this case has been considered, but in view of the experience at the second operation at which the adhesions were found to be so dense and extensive, and because of the inaccessibility of the site of the stricture, together with the fact that the patient gets along fairly comfortably with the use of the biliary drainage twice a week, it has been decided to treat the case conservatively.

COMMENT—In the case reported by Jones,⁴ the patient, a white woman, age 40, was crushed between two automobiles, the right upper abdomen and the right lower chest receiving the brunt of the trauma. She was unconscious at the time of injury, but shortly thereafter rallied and remained in comparative comfort for five or six days, by which time she had become jaundiced, the abdomen had become progressively enlarged, the patient was very weak, the urine contained bile, and the feces were clay colored. Paracentesis recovered 1,500 cc of thin bile. After several days' observation the patient was operated upon, at which time more than a gallon of bile was found in the abdomen, and a wound of the hepatic duct near its junction with the liver was identified. A drainage tube was inserted down to the site of the rupture and the gallbladder was also drained. One month after operation the drainage of bile from the wound had ceased, the jaundice had disappeared, and the stools were normal in color. She was discharged six weeks postoperatively, since which time she has remained entirely well.

Wallace and Spiro⁵ report the case of a male, age 47, who was crushed between two automobiles suffering trauma to the right costal region. When first seen he was in profound shock and complained of pain in the right hypochondriac region. On examination, there was external tenderness over the gallbladder area and the right upper rectus muscle showed marked rigidity. Liver dullness was normal. A tentative diagnosis of "rupture of the liver" was made. The shock was treated and the patient rallied within a few hours. Twenty-four hours after admission it was noted that he was slightly jaundiced, and this became progressively more marked from day to day. Two days after admission, bile was found in the urine. During the following 48 hours, the jaundice had become very intense, stools clay colored, and the urine was deeply stained with bile. Nine days after admission it was noted that the abdomen showed some general distention which was recognized as being due to an accumulation of fluid. By this time the patient's general condition was much worse, pulse rapid, tongue dry and coated, and he was growing rapidly very much weaker. Eleven days after the injury the patient's abdomen was opened through an upper midline incision and about three pints of bile were evacuated from the peritoneal cavity. At this point in the operation, the patient suddenly stopped breathing and all means of artificial respiration were of no avail. An autopsy showed several small tears on the anterior surface of the liver, all of which were healing. There was a large rent in the anterior layer of the lesser omentum near the attachment of the transverse fissure and, by careful dissection, a tear in the hepatic duct, which would admit the blunt end of an ordinary lead pencil was found. The edges of the hepatic duct were everted and there was some organization of the surrounding blood clot. Unfortunately there was no note made of the condition of the heart muscle, which would have been of considerable interest as it has frequently been claimed that profound jaundice causes some degree of myocarditis.

Edington⁶ reports the case of a male, age 24, who on September 16, 1931, was struck in the right upper quadrant of the abdomen by another man's head. The patient suffered a profound shock which

subsided rapidly within the course of a few days. Jaundice was notably shortly thereafter, together with pain in the lower abdomen. The jaundice gradually faded during the ensuing three weeks and the pain became much less. He returned to his occupation but found he was unable to work full time because of extreme weakness and lassitude, and at the end of the third week, it was noted that his abdomen was growing progressively larger. His stools by this time had become clay colored. On the fourth day after resuming work which was about three and one half weeks after the accident, he felt a sudden snap as though something had given way in the epigastrium. From this time on, the enlargement of the abdomen progressed very rapidly. At examination, after this episode, the patient was found to be jaundiced, the abdomen was distended but the flanks were tympanic. A fluctuant mass could be felt in the epigastrium. The diagnosis of "collection of fluid in the lesser sac" was made. Operation on October 15, 1931, one month after the injury, disclosed a large collection of fluid walled off behind the omentum probably in the lesser sac. This cyst like collection contained a large amount of dark greenish bile stained fluid. The edges of the cyst wall were marsupialized to the skin and the wound packed with iodoform gauze. A profuse and persistent discharge of bile followed the operation. The gauze pack was removed on the fifth day and the wound allowed to contract down to a fistula. Thirty three days after the operation bile was still discharging, and it was decided that a rupture of one of the bile ducts had occurred. The patient was reoperated upon and the fistulous tract, which led down to the region of the common duct was dissected free and anastomosed to the anterior surface of the stomach. The wound healed by primary union and from that time on the patient made an uneventful recovery. He was seen for the following nine months, during which time there was no recurrence of the symptoms and no evidence of stricture formation.

These reports could be continued, but they practically all show the same picture. The injury is always caused by crushing trauma to the right upper abdomen and the right lower chest. The patients are always in a marked degree of shock immediately after the accident, which, however, spontaneously subsides within a few hours and is followed by a period of relative freedom from symptoms except for localized pain for several days. Jaundice is usually the first secondary sign to appear, and is noted usually within the first three days. Bile in the urine also appears at about this time. Within the next week the stools have usually become clay-colored and there is a progressive and marked increase in the size of the abdomen, which on physical examination is found to be caused by an accumulation of fluid. By the end of the first week or ten days, the patient shows progressive loss of strength with a rapidly rising pulse, marked exhaustion and a moderate elevation of temperature. This picture, once seen, cannot be forgotten, and is pathognomonic of a laceration of one of the bile ducts. If there is any doubt, a paracentesis will disclose free bile present in the peritoneal cavity.

Treatment should consist of early celiotomy, before the patient has become too weak, evacuation of the bile, and simple drainage down to the site of the lacerated bile duct. Practically all of these lacerations heal spontaneously without necessity for repair, and in only a few instances have permanent strictures developed.

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wall to control bleeding from an adhesion. This condition proved to be quite stubborn, but ultimately healed after a period of five weeks' continuous suction of the fistulous tract. The jaundice spontaneously subsided, and it had entirely disappeared by April, 1932. As a result of the infection of the wound from the duodenal fistula, a ventral hernia developed, which was repaired in May, 1933.

Follow-Up—The patient has now been kept under observation for a period of over six years. Duodenal drainages are instituted once or twice a week, and if these are persisted in, the patient remains quite comfortable. There is always a residual jaundice which becomes intensified if the biliary drainages are allowed to lapse. Normal color is returned to the stools shortly after the second operation. The biliary drainages always produce a good quantity of golden-yellow bile, but no concentrated green bile is ever found.

About once every six months the patient has an attack of severe pain in the right upper quadrant of the abdomen, associated with a sudden increase in the intensity of the jaundice and a lightening in the color of the stools. There is usually a rise in temperature to 102° or 103° F. These attacks are relieved by hypodermics of morphine sulphate grains one-quarter, plus an icecap to the gallbladder region, followed shortly thereafter by duodenal drainage. One would assume that on these occasions the bile may become somewhat inspissated at the site of the stricture, causing a sudden complete obstruction with back pressure on the hepatic radicals in the liver. The attacks are always over within a day or two and do not recur with any great frequency.

Further exploration of the abdomen in this case has been considered, but in view of the experience at the second operation at which the adhesions were found to be so dense and extensive, and because of the inaccessibility of the site of the stricture, together with the fact that the patient gets along fairly comfortably with the use of the biliary drainage twice a week, it has been decided to treat the case conservatively.

COMMENT—In the case reported by Long,⁴ the patient, a white woman, age 40, was crushed between two automobiles, the right upper abdomen and the right lower chest receiving the brunt of the trauma. She was unconscious at the time of injury, but shortly thereafter rallied and remained in comparative comfort for five or six days, by which time she had become jaundiced, the abdomen had become progressively enlarged, the patient was very weak, the urine contained bile, and the feces were clay colored. Paracentesis recovered 4500 cc of thin bile. After several days' observation the patient was operated upon at which time more than a gallon of bile was found in the abdomen and a wound of the hepatic duct near its junction with the liver was identified. A drainage tube was inserted down to the site of the rupture and the gallbladder was also drained. One month after operation the drainage of bile from the wound had ceased, the jaundice had disappeared, and the stools were normal in color. She was discharged six weeks postoperatively, since which time she has remained entirely well.

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THE CLINICAL SIGNIFICANCE OF PANCREATIC REFLUX *

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Most observers now agree that the reflux of bile into the pancreas may find its clinical expression in acute pancreatitis under certain circumstances. On the other hand, the frequent occurrence of the reflux of pancreatic juice into the common bile duct has not been fully appreciated, and its clinical significance in many of the acute pathologic conditions of the biliary tract has not been properly evaluated.

When the choledochus and the duct of Wirsung terminate in a common ampulla—which is not uncommon—any factor causing occlusion of the papilla of Vater may convert both ducts into a common canal^{1, 2, 3}. This occlusion may be caused either by an edema of the papilla,⁴ or a muscular spasm of the sphincter of Oddi,⁵ or by a small gallstone impacted in the ampulla distal to the openings of the pancreatic and common bile ducts.⁶ Once this common channel has been established, the stage may be set for either biliary or pancreatic reflux. The direction of the reflux is undoubtedly dependent upon the relative intraductal secretory pressures, and inasmuch as this is usually higher in the pancreatic duct (unless the duct of Wirsung communicates with the duct of Santorini) a pancreatic rather than a biliary reflux is more likely to occur.

The amount of retrojected pancreatic juice into the bile, as determined by a quantitative estimation of the enzymes—either lipase, trypsin or amylase, will naturally vary tremendously. It will be dependent upon the secretory activity of the pancreas, the intraductal pancreatic pressure and the degree of obstruction at the ampulla.

The chemical recognition of these pancreatic ferments may present certain difficulties. The determination of lipase is not an easy procedure and has been attempted by but few investigators. The method for the detection of trypsin in the bile often presents several obstacles. An excess of protein and bile pigments, which may be present especially in pathologic bile, may destroy the accuracy of the determination. Trypsin deteriorates rapidly on standing, and, in addition, it is often in the inactive form and requires the addition of enterokinase for its activation.

These disadvantages have led most investigators to examine the bile for amylase as a quantitative index of pancreatic juice admixture. This enzyme is stable in bile and can be measured with comparative ease. However, two different types of amylase appear to be present in the bile. One type attacks

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the amylopectin which is present in soluble starch, and is mainly responsible for its viscosity. The other amylase, which may be present in a totally different proportion, attacks preponderantly the amylopectin converting it into maltose. Consequently the methods based on changes in viscosity of a standard starch solution (Davison,⁷ Elman,⁸ Crandall,⁹) will give results which may be totally different from either the method used to determine the end-point for the disappearance of the blue color due to iodine (Wohlgemuth¹⁰) or the methods based upon the measurement of the amount of maltose produced during a definite period of starch digestion (Willstätter¹¹, Schmidt¹²).

Human bile is ordinarily deficient in the liquefying amylase as measured by the viscosimeter method, and if this enzyme is found to be present it may be taken for granted that there is an admixture of pancreatic juice. This method, as modified by Elman, was, therefore, used in these analyses of bile.

The unit in this method is standardized as the amount of amylase which will reduce the viscosity of a standard starch solution 20 per cent in one hour's hydrolysis under controlled conditions. The starch solution is standardized so that 1 cc. of blood serum obtained from a number of fasting normal individuals will contain values falling between two to six units of amylase. If the enzyme is found in the bile in concentration above that obtained in the blood, it is reasonable to assume that a pancreatic juice admixture is present.

In the past, the possibility of the admixture of pancreatic secretion to the bile was only suspected when a rapid digestion and maceration of the skin about a biliary fistula suggested the presence of activated pancreatic enzymes. The paucity of clinical reports attests to the supposed rarity of this untoward complication. These pancreatic enzymes were presumably derived from either a duodenal reflux through the choledochostomy tube, or from a duodenal fistula, or from the pancreas by reflux. Postoperatively, the reflux of small intestinal contents through the common bile duct is exceedingly rare. The oblique implantation of the choledochus through the duodenal wall and the added protection of the sphincter mechanism make the reflux of duodenal contents through the common bile duct an uncommon occurrence. Codman,¹³ Davis,¹⁴ and Walters and Marshall¹⁵ have reported cases of this character, and only two cases similar in nature have been observed in our wards. The diagnosis of a duodenal reflux, however, should occasion very little difficulty. Walters¹⁵ states that one should become suspicious of this untoward complication when within 24 hours following a choledochostomy there is a discharge of a large amount of thin, fluid material with a rancid odor, or the skin about the drainage tube appears irritated and digested. If either methylene blue, or insoluble carmine crystals, which are administered by mouth, appear about the abdominal sinus or stain the drainage, the diagnosis is verified. On the other hand, if the drainage contains pancreatic ferments without signs of the orally administered dye, it is reasonable to suppose that a pancreatic reflux is present.

The appended case report (Case 1) graphically illustrates how the rapid

skin digestion about a choledochostomy sinus immediately suggested the possibility of a pancreatic reflux, which chemical analysis and clinical observation subsequently substantiated

Case 1—(No 375608) H H, a female, age 39, was admitted to the Mount Sinai Hospital January 12, 1935, and discharged February 6, 1935. A week prior to admission, the patient experienced an uncomfortable feeling in the back which was relieved by pressure. Five days later she began to complain of pain in the epigastrium, aggravated by food, and associated with nausea and vomiting. Simultaneously, the entire abdomen felt sore and the epigastric pain was aggravated by movement. There was no history of jaundice, chills or fever.

Physical Examination disclosed an acutely ill, subicteric female. There was tenderness in the right upper quadrant and the gallbladder was palpable. Icteric index, 31. White blood cells 14,300, polymorphonuclear leukocytes, 84 per cent, lymphocytes 14 per cent, hemoglobin, 90 per cent. The urine was clear, albumin, very faint trace, sugar, negative, bile, four plus, urobilin, one plus.

The patient was observed for 48 hours and then explored, under general anesthesia, through a six-inch, oblique, upper right rectus, muscle-splitting incision. The liver was slightly enlarged, but normal in size and consistency. The gallbladder was markedly thickened and acutely inflamed and measured about 7 cm. in length with an average diameter of 5 cm. It contained about 40 cc. of rather thin bile, and innumerable stones, several of which were found in the cystic duct. The gallbladder was adherent to the common bile duct, which was partially constricted by firm, dense adhesions. The choledochus contained no calculi. A typical retrograde cholecystectomy was performed. One tube was sutured to the cystic duct, which was left open, and another was placed into Morrison's pouch. The abdominal wall was closed in layers.

Postoperative Course—Four days postoperatively, the patient drained an unusually large amount of bile, and on the eighth day, a definite maceration of skin became apparent. Examination of the drainage fluid revealed large amounts of trypsin and amylase. There was no evidence of either a duodenal fistula or reflux, since ingested insoluble carmine failed to appear in the drainage. Two weeks later the drainage suddenly ceased and urobilin appeared in the stool.

In this case of pancreatic reflux it is possible that the bile and pancreatic ducts opened into a common ampulla which was subsequently occluded by either a small calculus or possibly by temporary spasm of the sphincter of Oddi. As soon as this obstruction was overcome, the bile and pancreatic juice emptied normally into the intestine, with immediate cessation of external drainage.

Recent studies have shown, however, that the occurrence of inactive pancreatic ferments in the bile due to reflux is not an uncommon occurrence. The admixture of pancreatic secretion, either in the bile of the choledochus or that of the gallbladder, may not be suspected because its presence may be perfectly innocuous and cause no recognizable clinical manifestations. Therefore, the frequency with which these pancreatic enzymes will be found in gallbladder and common duct fistula bile will naturally depend upon a routine analysis to establish their identity.

In a recent communication, Popper,¹⁶ using the Wohlgemuth method, examined the bile (usually from the gallbladder) in 219 surgical patients for the purpose of finding pancreatic ferments. The samples were obtained from

cases of cholelithiasis, tumors of the pancreas, acute pancreatic disease, and from those patients possessing a presumably healthy biliary system. Increased amylase was demonstrable in 17 per cent of the cases. Those in which the bile ducts contained pancreatic juice differed in no way from other cases of cholelithiasis in respect to history, symptomatology, clinical course, operative findings or postoperative course. Subsequent follow-up examinations, made months or years later, failed to reveal indications either of pancreatic or hepatic dysfunction.

In a series of 25 cases of chronic cholecystitis in which the gallbladder bile was routinely examined by us for amylase by the viscosimeter method no ferments were found, but in 12 cases of acute cholecystitis, large amounts of enzymes were present in four patients. In a routine analysis of the bile obtained from a choledochostomy drainage tube in 24 patients, amylase was present in eight. In six of these patients the pancreatic duct was visualized by lipiodol injections, and roentgenologic examinations by the following method.

About 12 days after a T-tube choledochostomy, iodized oil is injected by means of a 50 cc syringe through the drainage tube into the biliary tract. Under the fluoroscope the oil can be seen to enter the choledochus, fill the terminations of the hepatic ducts, and then pass through the sphincter into the duodenum. If the sphincter is spastic, the intrahepatic bile ducts are filled to a considerable extent before the oil is forced through the sphincter into the duodenum. At this point, anteroposterior and lateral roentgenograms are taken. Having made certain that there is no organic obstruction in the choledochus, morphine sulphate (Gr $\frac{1}{4}$) is administered hypodermically, and five minutes later iodized oil is again injected. The morphine induces a severe sphincter spasm,¹⁷ and as a result the entire biliary tract is usually visualized before the injected iodized oil can be forced into the duodenum. If the pancreatic duct opens together with the common bile duct above the spastic sphincter, the lipiodol will invariably enter the duct of Wirsung. This canal has been visualized fluoroscopically as far as the body of the pancreas in one case, and almost to the tail in another. Unfortunately, roentgenograms were not taken at this particular minute. Since the secretory pressure of the pancreas seems to be higher than the resistance of the sphincter of Oddi, only the terminal 5 to 7 cm. of the pancreatic duct may be visualized. Therefore, in order to demonstrate the pancreatic duct on the film, a steady continuous injection of lipiodol must be made while the plate is being exposed. At times when the sphincter is sufficiently spastic, the pancreatic duct may be visualized even before morphine is given (Figs 3, 5 and 8). The administration of this drug in such cases is not necessary and may even decrease the visualization of the pancreatic duct because it causes not only muscular spasm of the sphincter but also of the duodenal wall which embraces the ducts (Fig 4). Inasmuch as the abdominal orifice of the biliary fistula frequently overlies the region of the sphincter of Oddi, the patient should be turned over

slightly to the right in order to obtain an unobstructed view of the pancreatic duct

It might prove of interest to briefly abstract the histories of seven cases in which, in the course of a routine analysis of bile, the presence of amylase in sufficient concentration suggested a pancreatic reflux. In six of these cases the pancreatic duct was visualized.

Case 2 is of unusual interest because, at one time during the postoperative period, pure unactivated pancreatic juice was obtained from the choledochostomy tube. However, there were no clinical manifestations suggesting a pancreatic reflux other than the fact that the drainage was colorless in appearance and that its chemical analysis revealed amylase.

Case 2 — (No. 407176) M. F., a male, age 27, was admitted to the Mount Sinai Hospital April 15, 1937, and discharged June 3, 1937. The patient had been well until ten months before admission, at which time he began to develop postprandial sensations of burning in the epigastrium, accompanied by a feeling of distention and substernal pain. This would begin usually 15 minutes after a fatty meal and would last 15 minutes. Six days before admission, the patient experienced localized epigastric and substernal pain, and two days later he noticed jaundice, clay colored stools, and dark urine.

Physical Examination disclosed a jaundiced patient, not acutely ill. Abdominal examination was negative. Icteric index, 14. Blood bilirubin, 1.5 mg per cent, cholesterol, 319 mg per cent total, 115 mg per cent ester. Bile was present in the urine, and the stool contained no urobilin. Galactose and sodium benzoate tests were undertaken to rule out hepatitis. The galactose test gave an excretion of 3.5 Gm and the sodium benzoate 3.13 Gm, thus confirming the clinical impression of obstructive jaundice.

TABLE I
FRACTIONAL ANALYSIS OF FISTULA BILE OBTAINED FROM CASE 2

Date	Meal	Time of Bile Collection	Amylase Units per Cc
5/2/37 (11 days postoperative)	12 00 noon Lunch	2 30 P M	3,000
		4 30 P M	
	Supper	4 30 P M	1,255
		6 30 P M	1,000
		8 30 P M	1,800
		10 30 P M	2,000
5/3/37		12 30 A M	1,285
		2 30 A M	441
		4 30 A M	26
		6 30 A M	30
	8 00 A M Breakfast		
		8 30 A M	0
	11 30 A M Lunch	10 30 A M	300
		12 30 P M	2,000

Under observation, bile subsequently disappeared from the urine and urobilin was found in the stool

Operation April 21, 1937, revealed a chronically inflamed gallbladder containing a myriad of yellow, cholesterol stones. It was adherent to the duodenum and transverse colon. The common duct was dilated and inflamed and contained many small cholesterol stones. A retrograde cholecystectomy and a T-tube choledochostomy were performed.

Postoperative Course—Bile drained freely the day following operation. On the seventh day the bile drainage suddenly changed in character and about 250 cc of a colorless fluid was collected. This was analyzed and found to contain 7,000 Elman

FIG 1



FIG 2



FIGS 1 and 2—Case 2. Note that before administration of morphine (Fig 1) the hepatic ducts are only terminally outlined before lipiodol enters the duodenum. This indicates a normal resistance of the sphincter of Oddi. Five minutes after morphine administration, continued injection of lipiodol outlines the entire biliary tract and distends the common bile duct. In addition, the pancreatic duct (arrows) was outlined for considerable distance.

units of amylase. This fluid did not digest egg white, indicating that the trypsin had not been activated. The biliary drainage was analyzed daily, as well as for one 24 hour period for amylase (Table I). After two previous unsuccessful attempts, lipiodol visualization of the pancreatic duct was finally accomplished after producing spasm of the sphincter of Oddi by the hypodermic administration of morphine (Figs 1 and 2). The tube was removed on the thirty-ninth day and the external bile drainage ceased immediately.

Case 3—(No 416038) S. M., a male, age 52, was admitted October 30, 1937, and discharged December 7, 1937. There was a history of right upper quadrant pain which often radiated to the left upper quadrant and into the back. The pain was relieved by belching and by induced vomiting. There was no history of fever, chills or jaundice. The present episode began six days before admission and was similar to the previous attacks. The pain radiated from the right upper quadrant to the left upper quadrant and back.

Physical Examination revealed a thin, middle aged male. There were a few moist rales at the bases of both lungs. Tenderness and rigidity were present in the right upper quadrant of the abdomen, and a round ballotable mass was palpable in this region.

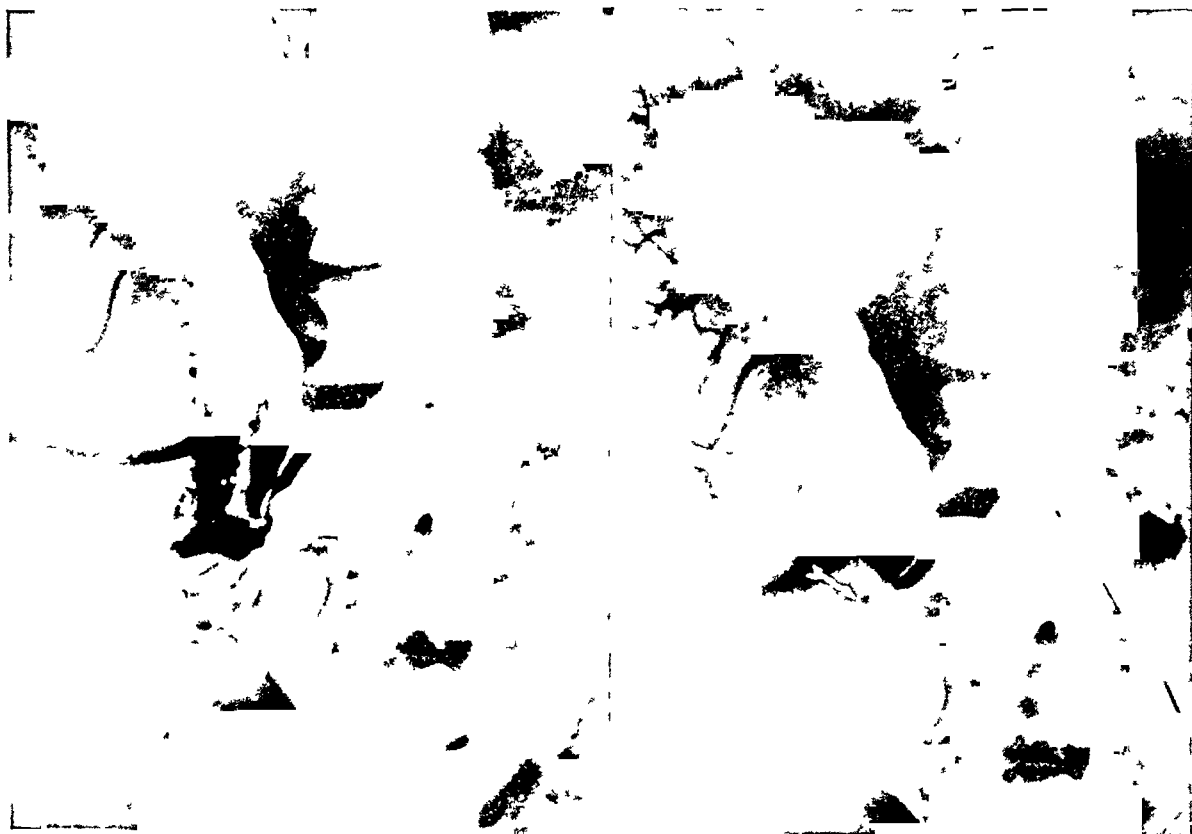
PANCREATIC REFLUX

Blood pressure 140/84 White blood cells, 14,000, 81 per cent polymorphonuclear leukocytes, 18 per cent lymphocytes Urine, negative for bile A scout roentgenogram of the abdomen revealed two ring-shaped concretions in the gallbladder region

Operation—October 10, 1937 A celiotomy, under spinal anesthesia, revealed an acutely inflamed, hydropic gallbladder containing two large stones impacted in the ampulla The common duct, which was dilated to three times its normal size, was the site of an acute inflammatory process and contained a small stone A cholecystectomy and a T-tube choledochostomy were performed

FIG 3

FIG 4



FIGS 3 and 4—Case 3 Injection of iodized oil showed considerable spasm of the sphincter of Oddi (Fig 3) since the hepatic ducts are outlined to a considerable extent before the oil passes into the duodenum At the same time a portion of the pancreatic duct (arrow) is filled The junction of the common and pancreatic ducts at the ampulla of Vater is clearly visualized Note also the dilatation of the common bile duct Following the administration of morphine (Fig 4) the whole biliary tract is outlined The increased tonicity of the duodenal wall as a result of morphine action caused compression of the intramural portion of both the common and pancreatic ducts The ampullary junction of these ducts are, however, still clearly outlined (arrow)

Postoperative Course—The patient's postoperative course was complicated by a bronchitis but was otherwise uneventful Bile drainage from the T-tube was positive for amylase Determinations varied between 15 and 85 units in 24 hour samples for 12 consecutive days Lipiodol roentgenograms of the biliary tract visualized the major hepatic radicles without the use of morphine The lipiodol could be seen passing into the pancreatic duct for a distance of about 10 cm (Fig 3) After the administration of morphine, the increased tonus of the duodenal wall partly obliterated the visualization of the intramural portion of both the choledochus and the pancreatic ducts (Fig 4) However, the ampulla at the junction of these two ducts was clearly visible On the thirty-seventh day, the T-tube was tied off At that time the sphincter resistance measured about 150 Mm After clamping the tube for five days, the resistance of the sphincter was found to be 90 Mm The tube was then removed and the fistula closed immediately

Case 4—(No 416858) M R, a married woman, age 62, was admitted to the private service of Dr Leon Ginzburg (through whose courtesy this case was studied) November 18, 1937, and discharged December 25, 1937 She suffered from an attack of

epigastric distress for the first time in August, 1936. In April, 1937, she again developed a very severe episode of epigastric pain radiating to both costal margins and the back. Administration of morphine was required. Since then the attacks had increased in frequency and severity, occurring as often as four times weekly. Pruritus and dark urine were present with each attack but jaundice was not noted until her present admission. At this time bile was present in the urine. The stool was clay colored and contained neither bile nor urobilin. Hemoglobin, 70 per cent, white blood cells, 38,000, 72 per cent polymorphonuclear leukocytes. Icteric index, 10.

Operation—November 29, 1937. A chronically diseased gallbladder containing stones was found. The choledochus was thickened and inflamed, and dilated to three times the normal diameter. An irregular shaped pigment stone about 1 cm. in diameter was found in the intramural portion of the common bile duct, and was extracted with some difficulty. Cholecystectomy and a T-tube choledochostomy were performed.

Postoperative Course—Five hundred to 700 cc. of a very pale, watery bile continued to drain daily for three weeks. Analysis of this revealed that it contained 1,200 units of amylase. It was felt that an obstruction was present, due either to the impaction of a residual stone at the papilla or to the presence of spasm of the sphincter of Oddi. The T-tube was clamped on the nineteenth day after operation for a short time, and bile passed into the duodenum without ensuing discomfort. It was clamped again for 24 hours on the twenty-third day. On the twenty-fourth day, lipiodol injection of the biliary tract revealed a spastic sphincter (Fig. 5), and visualization of the hepatic and pancreatic ducts was effected. The tube was clamped again on the twenty-fifth day and removed five days later, with the cessation of external drainage.

The following three cases are reported from the Ward Surgical Service of Dr. John Garlock, through whose courtesy these studies were made.

Case 5—(No. 416037). S. L., a male, age 58, was admitted October 30, 1937, and discharged November 30, 1937. For the past 38 years the patient had had recurrent attacks of rather vague, burning pain beginning at the angle of the right scapula and radiating around to the right upper quadrant. Six months before admission, he experienced a severe attack which was accompanied by a shaking chill and followed by jaundice, which lasted for one week. Roentgenologic examination at that time revealed incomplete visualization of the gallbladder but no stones. Similar attacks occurred two months, five days, and two days before admission.

Physical Examination revealed a well developed and well nourished male, definitely jaundiced. There was marked tenderness in the epigastrium and in the right upper quadrant. Temperature, 100.6° F., hemoglobin, 78 per cent. Blood chemistry, total cholesterol, 225, cholesterol ester, 56, icteric index, 10, bilirubin, 0.2 mg. per cent. Galactose tolerance test showed an excretion of 11 Gm. of sugar. Roentgenologic examination of the gallbladder by means of the Graham test failed to visualize the viscus.

Operation—November 8, 1937. The gallbladder was found thickened, shrunken, and full of calculi. The choledochus was not dilated, and revealed no stones. A probe passed easily into the duodenum. A cholecystectomy and a T-tube choledochostomy were performed.

Postoperative Course—Recovery was uneventful. Amylase was found in considerable concentration on several occasions, once as high as 75 units in a routine analysis of the biliary drainage. Activated trypsin was found once in the biliary drainage on the fifteenth day after operation. Roentgenologic examination of the biliary tract with lipiodol showed no dilatation of the biliary tract, an absence of stones, and a spasm of the sphincter of Oddi (Fig. 6). Following the administration of morphine, the pancreatic duct was visualized to the extent of 1.5 cm. (Fig. 7). The tube was removed on the nineteenth day, and the fistula closed almost immediately.



Fig 5

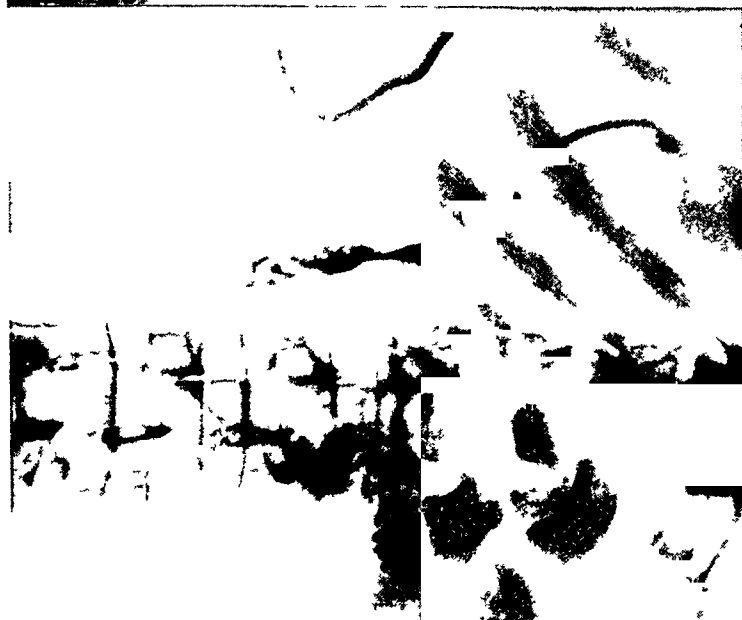


Fig 6



Fig 7

Fig 5—Case 4 Lipiodol visualization without morphine in this case clearly demonstrates a severe sphincter spasm present since the hepatic ducts are outlined to a very large extent before the iodized oil enters the duodenum. Enormous dilatation of the choledochus is noteworthy. The pancreatic duct (arrow) is outlined to considerable extent.

Figs 6 and 7—Case 5 Absence of sphincter spasm is noteworthy here. The iodized oil enters the duodenum without filling the hepatic ducts and without distending the choledochus (Fig 6). Following the administration of morphine (Fig 7) the whole biliary tract is outlined and the common duct is distended before lipiodol enters the duodenum. A small portion of the pancreatic duct is filled (arrow).

Case 6—(No 416741) Y S, a female, age 48, was admitted November 16, 1937, and discharged January 6, 1938. For the past two and one-half years she had experienced a pressing sensation in the epigastrium which radiated directly to the back. These episodes were usually preceded by a chilly feeling, and were accompanied by fever and severe nausea. They occurred two to three times a month and usually started one-half to one hour after eating. Jaundice was noticed only during the first attack. However, the patient noted that with each attack the urine turned dark and the stools were light in color. She had lost 35 pounds in weight.

Physical Examination—The patient was very thin and poorly nourished. The liver edge, which was hard and smooth, was palpable 10 cm below the costal margin. The spleen was just palpable. There was marked tenderness over the gallbladder region.

FIG 8



FIG 9



FIGS 8 and 9—Case 6. Injection of lipiodol shows presence of considerable spasm of the sphincter of Oddi (Fig 8) since the hepatic ducts are outlined to considerable extent before the oil can be forced into the duodenum. The choledochus is markedly distended. The pancreatic duct (arrow) is clearly outlined even the entrance of finer branches being shown. Following morphine administration (Fig 9) the whole biliary tract is outlined and the common bile duct is markedly distended. Increased tonus of the duodenum causes obliteration of the intramural portion of both common and pancreatic ducts. The pancreatic duct (arrow) is outlined only to a small extent.

Hemoglobin, 90 percent, white blood cells, 8,000, icteric index, 15, bilirubin, 3.5 mg per cent. Cholesterol total, 220 mg per cent, ester, 80 mg per cent. On the second day the patient experienced a severe attack of pain, accompanied by a chill and fever to 103° F. The next day, however, the icteric index was only 3, and remained low up to the time of operation. Sodium benzoate test showed a low excretion of 0.86 Gm of hippuric acid, indicating marked diminution in liver function.

Operation—November 26, 1937. Disclosed a chronically inflamed gallbladder without stones. The choledochus was thickened and dilated to 2.5 cm in diameter and contained nine large, black, crumbly, faceted stones. The papilla of Vater admitted the tip of the little finger. A cholecystectomy and a T-tube choledochostomy were performed. About 1,100 cc of bile drained the first two days but gradually diminished in amount. Amylase was found in the biliary drainage as high as 3,000 units on one occasion. Roentgenologic examination and lipiodol visualization on the twelfth postoperative day

demonstrated a dilated biliary tract with considerable spasm of the sphincter of Oddi. The pancreatic duct was clearly visualized, even some of the finer branches being filled (Fig 8). After increasing the sphincteric spasm by an injection of morphine, the entire biliary tract became outlined. The pancreatic duct was still visualized but to a lesser extent (Fig 9). The fistula closed almost immediately upon removal of the T-tube.

Case 7—(No 416700) I F, a male, age 54, was admitted November 15, 1937, and discharged December 16, 1937. He had been quite well until two months before admission when he suffered a very severe attack of right upper quadrant pain radiating to the epigastrium, back and right shoulder. This was accompanied by vomiting and jaundice. The attack recurred six weeks later and on the day before admission. He had lost 20 pounds in weight during the past two months.

Physical Examination revealed a well developed, rather obese, and markedly jaundiced male. There was moderate voluntary abdominal rigidity. The liver edge was palpable 2 cm below the costal margin. Hemoglobin, 90 per cent, white blood cells, 7,950, 59 per cent polymorphonuclear leukocytes. Liver function tests: Sodium d-lactate clearance test, normal, galactose test, normal. While under observation, the temperature rose to 101.5° F. Bile and urobilin were present in the urine. Icteric index, 23, bilirubin, 5.0 mg per cent, total blood cholesterol, 270 mg per cent, ester, 79 mg per cent.

Operation—November 22, 1937. Revealed a thickened, edematous and somewhat inflamed gallbladder with stones, adherent to the second portion of the duodenum. The choledochus was thickened and moderately dilated. It contained yellowish white thick purulent material and one small faceted stone in the distal portion of the duct. A large probe passed into the duodenum without difficulty. A cholecystectomy and T-tube choledochostomy were performed.

There was drainage of only small amounts of bile which frequently contained amylase. Bile samples collected every six hours during a 24 hour period (Table II) showed an amylase concentration of 1,500 units. No activated trypsin was found.

TABLE II
FRACTIONAL ANALYSIS OF FISTULA BILE OBTAINED FROM CASE 7

Date	Meal	Time of Bile Collection	Amylase Units per Cc
12/9/37 (7 days after operation)	12 00 noon Lunch	1 30 P M	1,200
		4 30 P M Supper	
		6 00 P M	1,500
12/10/37		12 00 midnight	0
		4 00 A M	1 5
		7 00 A M	0

Postoperative Course—The jaundice cleared up slowly. On the sixteenth day, the biliary tract was examined roentgenologically after the injection of lipiodol. Under the fluoroscope, the sphincter was seen to be definitely spastic, and the common duct slightly distended, the hepatic ducts were, however, markedly dilated (Fig 10). After administration of morphine, the pancreatic duct was seen to fill as far as the tail of the pancreas. However, during the few moments consumed placing the cassette in position, the pancreatic duct emptied almost completely and only about 5 cm were demonstrable (Fig 11).

The T-tube was removed on the twenty-third day and the fistula closed almost immediately.

The rôle of spasm of the sphincter of Oddi in the production of a pancreatic reflux is further substantiated in the appended report (Case 8). The pancreatic duct was not visualized in this patient, possibly because morphine was not used.

Case 8—(No 382140) C. F., a female, age 60, was admitted July 12, 1935, and discharged August 27, 1935. She had suffered from attacks of gallbladder pain for five years. Jaundice accompanied the last episode, which occurred 12 days after operation. The icteric index at the time was 50, and the bilirubinemia 2.0 mg per cent.

Operation—July 20, 1935. The gallbladder was found full of stones and acutely inflamed. The common duct was thickened, enlarged to twice its normal diameter, and

FIG 10

FIG 11



FIGS 10 and 11—Case 7. Before the administration of morphine (Fig 10) injection of oil fills the hepatic ducts to considerable extent indicating sphincter spasm. Five minutes after morphine administration (Fig 11) the hepatic ducts are outlined to a greater extent. A considerable portion of the duodenum is clearly outlined. At the same time a portion of the pancreatic duct (arrow) is filled

filled with a sand-like precipitate, but contained no stones. A retrograde cholecystectomy, and a choledochostomy, were performed.

Postoperative Course—Urobilin was not present in the stools until the nineteenth day. Pancreatic enzymes, trypsin and amylase, were demonstrated in the biliary drainage on several occasions. On the third day the initial resistance of the sphincter was 225 Mm H₂O, and thereafter was constant at 185 Mm H₂O. On the sixth day after operation, the constant resistance was even higher, remaining at 220 Mm H₂O. On the tenth day the injection of lipiodol outlined the hepatic ducts extensively, and only a few droplets of lipiodol entered the duodenum. The following day no lipiodol was evident in the duodenum, but some still remained in the choledochus, while the remainder was seen in the drainage.

The kymographic studies in this case, without the use of morphine, indicated a periodic spasm of the sphincter which was further substantiated by

lipiodol studies The presence of amylase was indicative of pancreatic reflux, even though the pancreatic duct was not visualized in the roentgenograms

A study of Cases 2, 3, 4, 5, 6, 7 and 8, in which the presence of a pancreatic reflux was first demonstrated chemically, emphasizes, quite clearly, the importance of spasm of the sphincter of Oddi not only in causing an obstruction at the papilla, but simultaneously converting the biliary and pancreatic ducts into one continuous channel Archibald,⁵ in his studies on biliary reflux in the production of acute pancreatitis, first suggested the possibility that spasm of the sphincter of Oddi alone was sufficient to convert the choledochus and duct of Wirsung into one canal, provided they both opened into a common ampulla, proximal to the sphincter He submitted certain evidence gained from animal experiments to substantiate his contention This work was not confirmed by Wangenstein and his associates,¹⁸ and others, who stated that they were unable to produce the regurgitation into the pancreatic duct without organic obstruction at the papilla

These cases certainly seem to confirm the fact that in the human, spasm of the sphincter alone is sufficient to convert the pancreatic and biliary ducts into one canal and establish a basis for either a pancreatic or biliary reflux In addition, these cases also seem to prove the postulate of Popper,¹⁶ who, from his extensive investigations on pancreatic reflux, stated that if high concentrations of pancreatic enzymes were found in the bile, a direct anatomic communication between the biliary and pancreatic ducts could be predicted This was found to be true, for in six of the seven cases of pancreatic reflux, the duct of Wirsung was visualized roentgenologically after the injection of lipiodol into the common bile duct

However, the admixture of pancreatic juice with the bile seems to vary periodically in the same patient, because there were times in which the ferments were found to be absent (Tables I and II) If the bile is to be analyzed for amylase, specimens should be obtained after the ingestion of a well balanced meal The presence of large amounts of pancreatic ferments in the bile did not seem to occasion any special symptomatology in these cases In Case 2, drainage at one time was pure, inactivated pancreatic juice and yet no significant clinical manifestations were recognizable Apparently, under certain circumstances, inactivated pancreatic juice appears just as innocuous, and apparently as harmless, as it is in the duct system of the pancreas In fact, the choledochus itself seems particularly immune to the necrotizing effects of an admixture of bile and pancreatic juice Benign strictures of the common bile duct, either noncongenital in origin, or unassociated with gallstones, are rarely found at a primary operation Moreover, the follow-up studies of all the cases in this series associated with a pancreatic reflux presented no subsequent complications referable to common duct involvement It may be argued, and justly so, that the reflux of pancreatic juice in the postoperative group of cases was caused artificially by the choledochostomy and that in the presence of an intact common bile duct, this reflux would not have occurred This may be partially true For it is

more likely that the pressure in the common bile duct may have been sufficiently lowered by the institution of the T-tube drainage so as to have favored the flow of pancreatic juice over the choledochus. However, in another group of acute cases which will be discussed later, the bile removed from either the peritoneal cavity or gallbladder at the time of operation occasionally revealed pancreatic ferments in such high concentrations that their presence can only have been accounted for on the basis of a pancreatic reflux. This group is composed of those cases of nonperforative biliary peritonitis and certain types of acute cholecystitis.

Bile peritonitis without demonstrable perforation of bile passages was first reported by Clamont and Von Haberer,¹⁹ in 1910. They suggested that this might have been caused by an alteration in the permeability of the bile duct walls, permitting the bile to seep through. Blad²⁰ subsequently offered an explanation for these unusual phenomena on a basis of his chemical and animal experiments. He felt that the pancreatic ferments, aided by bacterial action, digested the colloids of the bile and liberated the bile pigment which, by some unknown process, could then pass through any membrane. Wolfer²¹ was subsequently able to experimentally produce pathologic changes in the gallbladder wall by the injection of various amounts of pancreatic juice. He recently reviewed the literature of nonperforative bile peritonitis and presented several cases with interesting chemical findings.²²

The following case, observed by us, graphically illustrates a bile peritonitis without demonstrable perforation of the bile passages in which not only were areas of fat necrosis present in the peritoneal cavity, pointing to the presence of pancreatic enzymes in the free bile, but, in addition, trypsin and amylase were present in the bile aspirated from the gallbladder at the time of operation.

Case 9—(No. 402601) P. G., a female, age 45, was admitted December 22, 1936, and discharged January 23, 1937. During the past three years, she had experienced 15 to 20 attacks of severe, squeezing, epigastric pain, radiating both to the left and to the right, and to the middle of the back. Pain persisted and she had vomited once. There was no history of jaundice, acholic stools, dark urine, fever or chills.

Physical Examination disclosed a well developed female, apparently acutely ill. Temperature, 98.6° F. Blood pressure, 150/90. The abdomen was slightly distended. There was slight, diffuse abdominal resistance, most marked in the left flank, and marked tenderness in the epigastrium and right upper quadrant with slight rebound tenderness. White blood cells, 33,900, 95 per cent polymorphonuclear leukocytes. The urine showed urobilin 1:100. Icteric index, 5, blood bilirubin, 0.8 mg per cent, van den Bergh direct, promptly positive, indirect, 1:125,000.

Inasmuch as the physical signs and symptoms persisted, an abdominal puncture was performed ten hours after admission. This revealed bile-tinged hemorrhagic fluid which on smear showed leukocytes, but no organisms. In view of the presence of bile in the abdominal fluid, the possibility of a perforation of the gallbladder was considered.

Operation—Dr. Amiel Glass. The gallbladder, which was not inflamed, was found markedly distended by a small amount of clear, green bile and several hundred small yellow stones. There was a large quantity of apparently nonpurulent bile in the general peritoneal cavity, and bile seemed to issue from the foramen of Winslow. There were five to six small points of fat necrosis on the peritoneum and omentum adjacent to the head of the pancreas. This was slightly enlarged and blood stained bile was present beneath its peritoneal covering. A cholecystostomy was performed.

The gallbladder bile aspirated at operation showed the presence of both amylase and trypsin. A fragment of omentum removed at operation showed fat necrosis histologically. The stools were immediately positive for urobilin.

Postoperative Course—The patient did well postoperatively. There was free biliary drainage at first which gradually ceased. The patient was discharged 31 days after operation.

The other type of acute case associated with pancreatic reflux is acute cholecystitis. Clinically, considerable quantities of active pancreatic ferments have been found in the bile obtained from acutely inflamed gallbladders, and their presence appears to be definitely related to the acute inflammatory process present. Such instances have been reported by Bundschuh,²³ Ruppanner,²⁴ deDziembowski,²⁵ and Brackertz.²⁶ Three similar cases of acute cholecystitis associated with the presence of appreciable quantities of pancreatic enzymes in the gallbladder bile have been previously reported from the Surgical Services at the Mount Sinai Hospital.²⁷ In two of these cases, surgical exploration disclosed free bile in the peritoneal cavity, and in one, fat necrosis was seen not only in the acutely inflamed gallbladder wall, but also in the adherent omentum. The gallbladder bile which was aspirated at the time of operation was definitely alkaline, and diastase was present in large amounts in all three cases. The cultures were sterile in two cases, but in the third, *B. coli* and *B. Friedlander* were present. No bacteria were found in the microscopic sections of the gallbladder in any of the three cases. The pancreatic ferments present in the gallbladder bile could have been accounted for only by pancreatic reflux.

The exact mechanism by which pancreatic ferments in the bile may be perfectly innocuous under certain circumstances, and in others cause either a nonperforative bile peritonitis or acute cholecystitis, is not definitely known. The experimental work of Wolfer,²¹ Diagstedt,²⁸ Ivy,²¹ Andrews,²⁹ and others, show that the local cytolytic action of bile salts, the alkalization of the gallbladder bile, and the presence of appreciable amounts of pancreatic ferments and infection, are all factors in the alteration of the permeability of the gallbladder wall, and in the production of acute cholecystitis.

CONCLUSIONS

The presence of amylase in significant amounts in the biliary drainage predicates a pancreatic reflux which may be due solely to a spasm of the sphincter of Oddi. This spasm produces not only an obstruction at the papilla, but simultaneously converts the bile and pancreatic ducts into one continuous channel. Under these circumstances, the injection of lipiodol through the biliary fistula may visualize the pancreatic duct.

Pancreatic ferments in the bile may occasion no recognizable clinical symptoms. The common bile duct appears particularly immune to the effects of pancreatic ferments, but the presence of pancreatic juice in the gallbladder may produce either a nonperforative bile peritonitis, or an acute cholecystitis.

The mechanism which precipitates these acute inflammatory reactions is not clearly understood

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DISCUSSION—DR ALLEN O WHIPPLE (New York) expressed his particular appreciation of Doctor Colp's paper and felt that it was an exceedingly important addition to the current knowledge of biliary and pancreatic pathology. Undoubtedly if the type of clinical investigation that Doctor Colp had put into these cases were carried out more methodically the number of cases in which pancreatic ferments are found in both the gallbladder and common duct would be surprising. Doctor Whipple could recall at least five personally observed instances in which, chiefly because of the digestion of tissue in the common duct tract, pancreatic ferments were discovered, and in those cases it was impossible to recover carmine particles given by mouth. He feels certain that they were examples of pancreatic reflux.

Two features about this condition, however, appear to cloud the issue. One is the lack of definite knowledge regarding the mechanism activating the ferments. One of his problems, when trying to demonstrate the pathologic picture and findings of acute pancreatitis in cats for third year medical students, is the marked variation in one's ability to produce it. In some animals it can be produced by means of bile, in others it is not even possible even though bile is injected directly through the pancreatic ducts. The most constant method of producing it is by the mixing of duodenal contents with the bile. But bile in itself will not always effect it, which, Doctor Whipple thought, accounted for the fact that in many of these cases pancreatic juice coming out of the fistula is not activated and unless it is tested for ferments one would not suspect it to be a pancreatic reflux.

The other difficulty is to explain why, with the administration of morphine, which is so regularly used in postoperative work, particularly in biliary tract surgery, there is not more evidence of common duct dilatation and damage to the biliary tract. The strongest proof—and it is incontestable proof—that one does get a spasm of the sphincter was shown by the roentgenologic studies made by Doctor Colp, an observation noted by others.

Doctor Whipple was not altogether in agreement with Doctor Colp in the assumption that lesions in the common duct are not found as a result of pancreatic reflux. He recalled four cases, in three of which he assisted at the operation so that he could vouch definitely for the fact that the common duct was not injured during the course of the operation, that subsequently developed a type of stricture of the common duct that was utterly irreparable. At the time of operation later, when the patients had become deeply jaundiced, it was impossible to find anything but a strand of dense connective tissue extending from the duodenum right up to the portal fissure. At times activated pancreatic ferments may effect considerable damage to the common

duct—the only explanation for the extensive and diffuse destruction of the common duct in the four cases cited. It would seem possible that pancreatic reflux could damage the common duct inasmuch as it certainly produces tissue necrosis in some cases where the pancreatic juice with pancreatic reflux is activated.

Doctor Whipple expressed again his appreciation and admiration for the type of clinical investigation done by Doctor Colp. These studies and such studies as those by Wolfser and Dragstedt and Andrews, the Chicago group which has been very active in the study of the chemical production of acute cholecystitis (Doctor Whipple felt that many cases of acute cholecystitis were not bacterial but were definitely of a chemical origin) are supplying not only interesting pathologic data but observations which are exceedingly practical from the surgical standpoint.

DR MORRIS K. SMITH (New York) thought that Doctor Colp's cases demonstrated clearly the reflux of pancreatic juice into the biliary system and bile into the pancreas, as the result of spasm of the sphincter of Oddi. His sphincterotomy and its successful use in a most difficult case were impressive. That spasm of the sphincter of Oddi may be the cause of some attacks of pain after cholecystectomy sheds light on a perplexing problem. At the Mayo Clinic they have been able to relieve some such attacks with amyl nitrite. Doctor Colp showed an operative procedure that has been followed by relief for a year. If further experience is likewise favorable without undue hazard it would seem to be a valuable contribution to biliary surgery.

DR HENRY F. GRAHAM (Brooklyn) stated that he had performed one transduodenal choledochotomy for a large stone impacted in the ampulla of Vater. What he remarked particularly was the violent hemorrhage that occurred as he incised the posterior wall of the duodenum over the stone. The sphincterotomy looks like a very efficient instrument but it certainly looks vicious, too. He wondered if there were not some danger of incising one of the large vessels in the operation described by Doctor Colp. Another possibility would be too perfect healing of the incision. Would it not be possible to prevent bleeding and maintain the large opening by passing a good sized tube down the common duct through the sphincter and into the duodenum, bringing the other end out through the wound in the skin? This could easily be removed in a week or so when healing has progressed sufficiently. Doctor Graham said he had used this method without incising with the sphincterotomy. Dilators were passed and the sphincter was further stretched by a clamp, a tube was then passed, in order to maintain the dilatation. An 18 or 20 F catheter can often be used.

DR SEWARD ERDMAN (New York) appreciated Doctor Colp's interesting research and ingenuity in cutting the sphincter of Oddi, and his theory that the admixture of pancreatic ferments with the bile may be a factor in the production of acute cholecystitis. A number of theories have been adduced to explain the swollen, edematous, acute gallbladder, which is so often sterile so far as bacterial cultures are concerned. One of these is that pressure of a stone impacted in the cystic duct may so compress adjacent veins that edema and even gangrene may result. Perhaps, as Doctor Colp showed, in some cases the inflammation is chemical in origin and results from the presence of the pancreatic ferments.

As for the action of morphine, which Doctor Colp claimed causes more spasm of the sphincter of Oddi and increased tension in the ducts, it is difficult to explain the commonly observed fact that a single good dose of mor-

phine usually relieves not only the immediate pain, but ends the attack. If during the period of action of the morphine, the duct tension remains raised, the patient should awake from the effects of the drug with the same or an increased amount of pain.

As for the wide adoption of cutting the sphincter of Oddi one must await later reports concerning its ultimate benefits, for it is possible that after full healing and cicatrization an actual constriction might result, for even the powerful sphincter ani, if cut clean through at a right-angle to the fibers, usually heals without loss of its sphincteric action, despite the tremendous pressures to which it is daily subjected.

Lahey has found that dilatation with sounds is a satisfactory method of overcoming a tight sphincter of Oddi, and this would seem to be a simpler and safer procedure than section.

Doctor Erdman believed that Doctor Colp's case in which numerous adhesions in the upper abdomen were separated, may have received some of the benefit derived from the removal of the adhesions.

DR RALPH COLP (closing), was very much interested in Doctor Whipple's remarks concerning the occurrence of strictures in the common bile duct as possibly being due to a pancreatic reflux. He had previously asked Dr Ellsworth Eliot, who had collected a large series of cases of benign strictures of the common bile duct, whether he had ever encountered a case in which at the primary operation there was a stricture of the common bile duct which was not congenital in origin and was not associated with gallstones and which possibly may have been associated with a pancreatic reflux. He stated that he had not been able to find one. If the common bile duct were attacked through the medium of a pancreatic reflux, Doctor Colp thought that patients clinically exhibiting enzymes in the bile might subsequently return with some signs referable to stricture of the common bile duct. This has not occurred in Popper's series or in theirs. It is unquestionably true that the alkalinity present in acute gallbladders in which pancreatic enzymes are found undoubtedly plays a rôle in the production of the acute chemical inflammation, and one would naturally expect to find a similar reaction in the common bile duct in which the bile is usually alkaline. However, Doctor Colp had never seen an acute cholelithiasis associated with a pancreatic reflux.

Doctor Colp said that he surely had not meant to imply that he would not use morphine in acute gallbladder colic just because it causes a spasm of the sphincter of Oddi. Primarily, morphine is administered because it relieves pain, regardless of what it does to the sphincteric mechanism. It is quite evident from kymographic tracings that morphine causes contraction of the smooth muscle of the sphincter of Oddi, and also of the duodenum. Drugs like papaverin and various others had been administered with the idea of relieving pain without causing a spasm, but up to the present time Doctor Colp had not found this possible.

In this series of cases the incidence of spasm of the sphincter of Oddi, converting the pancreatic and common bile duct into a single channel, was found greater than originally reported. Mann and Giordano claimed that from their studies on cadavers that the anatomic variations making possible a pancreatic reflux, occurred only in 3.5 per cent of their cases. Yet Cameron and Noble, by pouring Wood's metal into the choledochus after occlusion of the papilla with a small stone, were able to demonstrate the pancreatic duct in the mold in over 75 per cent of their preparations. In the 24 cases of common bile duct drainage, which were routinely analyzed for pancreatic ferments, enzymes were found in 33 per cent of the cases. If pancreatic secre-

tion may be present in the common bile duct under certain circumstances, then the reverse may also be true, namely, that bile may be found in the duct of Winsung more frequently than heretofore supposed

No one would advocate the promiscuous division of the sphincter of Oddi. The patient presented was thoroughly studied by Dr. Isidore Feder of Brooklyn, and was given every opportunity for improvement with medication and dietary regimen before endocholedochal sphincterotomy was performed. Doctor Colp could not agree with Doctor Erdman that the adhesions which were found at the time of operation could possibly have caused the attacks of colic. He did not believe that the simple division of these adhesions would have relieved, so satisfactorily, these episodes which so closely simulated biliary colic. Apropos of the question of stricture following endocholedochal sphincterotomy, he said that the sphincter had been divided in another case which subsequently came to autopsy a year later. The incision in the anterior portion of the sphincter was well healed and the papilla was wide open. There is always the possibility, however, that a stricture may develop, but Doctor Colp could not see why this should occur. In other regions of the body in which a sphincter is divided in a single plane, strictures do not result. On the other hand, he thought the forceful dilatation of the sphincter of Oddi with a sound from which multiple tears might result, was fraught with greater danger of a subsequent stricture than after performing a sphincterotomy. However, one cannot deduce too much from this one case. Cases of true sphincteric spasm are comparatively rare and surgical division of the sphincter should be performed only when all other therapeutic measures have failed. In answer to the question raised by Doctor Graham as to danger of hemorrhage of the divided sphincter, Doctor Colp stated that this procedure of endocholedochal sphincterotomy had been performed on many cadavers and they were unable to find that any vessel of appreciable size had been divided. The suggestion of putting a tube in the common duct and passing it through the sphincter of Oddi to act in an hemostatic capacity is a very good one. There is another method of dividing the sphincter. Doctor Archibald told him he had employed it in several cases by a simple technic. He introduced a probe down into the common duct to the papilla. The papilla was then elevated against the anterior duodenal wall and a small incision was made into the bowel in this area. The sphincter of Oddi, which was easily visualized, was then divided and the duodenum subsequently entered. Doctor Colp said he preferred not to incise the duodenum unless it is absolutely essential, because, aside from the possibility of a fistula, a troublesome deformity might result. It would appear that this method of endocholedochal sphincterotomy should receive further trial in suitable cases.

STUDIES ON RENAL HYPERTENSION*

THE EFFECT OF DEVIATING URINE INTO THE BLOOD STREAM AND
INTESTINES OF DOGS

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THE present experiments were undertaken in order to throw some light on the pathogenesis of renal hypertension. It is now well established that elevation of the arterial blood pressure can be produced in animals by various procedures which decrease the blood flow through the kidneys. Thus, partial ligation of the renal arteries (Janeway,¹ 1909, Hartwich,^{2, 3} 1929, and Friedman,⁴ 1930), constriction of the renal veins (Bell and Pederson,⁵ 1930, and Menendez,⁶ 1933), the production of interstitial fibrosis in the kidneys by exposure to roentgen rays (Hartman, Bolliger, and Doub,⁷ 1927), compression of the renal arteries with adjustable clamps (Goldblatt, Lynch, Hanzal, and Summerville,⁸ 1934), and the ligation of one or both ureters (Hartwich,^{2, 3} and Harrison, Mason, Resnik, and Rainey,⁹ 1936), have each been found to cause a rise in the blood pressure. In some of these experiments hypertension has been maintained for long periods of time^{5, 7, 8}. The mechanism by which changes in the kidney or in its blood supply produce this abnormal rise in blood pressure has aroused great interest but is still not entirely understood.

A reflex effect from the ischemic kidney appears to have been ruled out as the cause of this type of hypertension by the findings that it is not prevented or relieved by denervation of the kidneys (Page,¹⁰ 1935, and Collins,¹¹ 1936), excision of the splanchnic nerves (Goldblatt,¹² 1936), or complete sympathectomy (Alpert, Alving, and Grimson¹³). Furthermore, hypertension has been produced by constricting the blood supply to a single kidney transplanted to the neck (Blalock and Levy,¹⁴ 1937) or to the groin (Glenn, Child, and Heuer,¹⁵ 1937). There remains the possibility that some chemical substance is absorbed from the ischemic kidney and that this exerts a pressor effect upon the endings of the vasoconstrictor nerves or directly upon the blood vessels. Such a substance might conceivably appear in the blood stream as a result of normal metabolic processes and fail to be adequately excreted by the damaged kidneys or it might be produced locally by the ischemic organs. In either case it would be expected to accumulate in the blood and perhaps be found to a certain extent in the urine or in extracts of the kidneys.

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In the present experiments, the urine from one or both kidneys has been deviated either directly into the blood stream or into the intestines, and observations made as to the effect of these procedures upon the blood pressure and general health of the animals. It has been well established that following bilateral nephrectomy the blood pressure does not rise above normal during the few remaining days of life (Blalock and Levy,¹¹ 1937). This experiment suggests that retention of waste products normally excreted in the urine does not produce a pressor effect. On the other hand, the observation that ligation of the ureters commonly results in a definite hypertension^{2, 3, 9} indicates that the kidneys may normally add some pressor substance to the urine which is reabsorbed under these conditions.

Observations on the Effect of the Chronic Reabsorption of Urine from the Intestines upon the Blood Pressure—When both ureters are implanted into the duodenum of dogs, the urine is almost completely reabsorbed, the non-protein nitrogen of the blood rises to very high levels, and the animals die within a relatively few days of uremia (Baird, Scott, and Spencer,¹⁶ 1917, and Hinman and Belt,¹⁷ 1922). Deviation of the urine from both kidneys into the lower small intestine, however, is tolerated fairly well for relatively long periods even though considerable elevations in the blood urea indicate continuous reabsorption of at least part of the urine (Bollman and Mann,¹⁸ 1927). A variation of this latter method was employed in the present experiments. Healthy adult dogs were selected, and all operations were performed under ether anesthesia, and with the usual aseptic precautions. The bladder neck was crushed, transected, and ligated, thus freeing it from the urethra, a wide lateral anastomosis was then made between the fundus of the bladder and the ileum about 12 cm from the ileocecal valve. This procedure was found to be superior to direct implantation of the ureters into the intestine because of the high incidence of partial ureteral obstruction with the latter method. Determinations of the blood pressure were made by inserting a needle connected with a mercury manometer directly into the femoral artery. The non-protein nitrogen of the blood was determined in the usual way. Significant results were obtained with four animals. Recovery from the immediate effects of the operation was usually prompt and complete. A diet of ground beef, bread, and milk was provided, but three of the animals ate very little, became progressively emaciated, and died or were destroyed in 20, 23, and 28 days, respectively. One animal took food regularly and survived for 89 days when he contracted distemper and was electrocuted. A definite and sustained elevation in the nonprotein nitrogen of the blood occurred in each case following operation, but in all the postoperative blood pressure readings were lower than the preoperative controls. The details of these experiments are given in the following summarized protocols.

Dog No. 1—Control blood pressure was 130 Mm Hg and the NPN of blood 38 mg

Operation—Lateral anastomosis between the bladder and lower ileum. Following operation the animal very largely refused food and became increasingly cachectic. On the sixteenth postoperative day the

blood pressure measured 110 Mm Hg, and the blood N P N was 50 mg per cent. The animal died on the twentieth day. Autopsy revealed a patent anastomosis between the bladder and ileum, and the kidneys and ureters appeared grossly normal. Microscopic examination of the kidneys revealed moderate hyalin changes in the tubules and glomeruli and slight fatty infiltration.

Dog No 2—Wt 110 Kg. The preoperative blood pressure was 120 Mm Hg, and the blood N P N 32 mg.

Operation—Lateral anastomosis between the bladder and the lower ileum. On the eighteenth day after operation the N P N was 107 mg, but the blood pressure had decreased to 112 Mm Hg. The animal became progressively weaker and emaciated and died on the twenty third day, weighing at this time only 67 Kg. At autopsy the kidneys and ureters were found to be normal on both gross and microscopic examination. The anastomosis was patent. A small fistulous tract was present between the bladder and urethra.

Dog No 3—Wt 128 Kg. The preoperative control blood pressure readings averaged 150 Mm Hg, and the N P N was 35 mg per cent.

Operation—Lateral anastomosis between the bladder and lower ileum. This animal took his food fairly well and remained in good physical condition. On the fourteenth postoperative day the blood pressure was 130 Mm Hg, and the N P N 45 mg, on the thirty seventh day the blood pressure was 140 Mm Hg, and the N P N 54 mg, on the fifty second day the blood pressure was 130 Mm Hg, the N P N 73 mg, and the weight had decreased to 75 Kg, on the sixty fifth day the blood pressure was 106 Mm Hg, the N P N 79 mg, and the weight had increased to 87 Kg, and on the eighty ninth day the blood pressure was 112 Mm Hg, the N P N 72 mg, and the weight 88 Kg. The animal was electrocuted because of distemper on the eighty ninth day after operation. At autopsy the anastomosis was patent and the kidneys and ureters appeared grossly normal. On microscopic examination the kidneys displayed occasional areas of hyalin degeneration, but were otherwise normal. The aorta, peritoneum, spleen, liver, adrenals, heart, and lungs were grossly normal.

Dog No 4—Wt 112 Kg. The preoperative blood pressure was 130 Mm Hg.

Operation—Lateral anastomosis between the bladder and the terminal ileum. On the fifteenth day after operation the blood pressure measured 100 Mm Hg. On the nineteenth day the N P N was 60 mg, and on the twenty eighth day 57 mg per 100 cc. On the twenty eighth day the animal developed distemper and was electrocuted. The anastomosis was found to be patent and the ureters and kidneys appeared normal on gross inspection.

The experimental data, while not extensive, were sufficiently uniform to prove that the continuous partial reabsorption of urine from the alimentary tract in dogs does not produce hypertension. The amount of reabsorption was sufficient to maintain a persistent elevation of the blood nonprotein nitrogen at about twice the normal level. Clinical evidence of a chronic toxemia was also present as evidenced by the persistent anorexia, depression, and marked loss in body weight.

Observations on the Effect of Deviating the Urine from One Kidney Directly into the Circulation—Absorption from the gastro-intestinal tract is well known to be a selective process and the possibility remained that some pressor substance excreted with the urine failed to be reabsorbed by the intestinal mucosa in the preceding experiments. To test this possibility, a direct anastomosis was made between the ureter from one kidney and a convenient vein, usually the lumbar vein or the inferior vena cava. This procedure has been reported, by a number of authors, to cause a rapidly fatal toxemia, and the existence of a specific nephrogenic toxin has been postulated to account for the result. Since the literature in this field is conflicting and since the possibility of such a specific substance of renal origin is of considerable significance in the present problem, the previous work will be briefly reviewed.

Brucke,¹⁹ in 1926, was apparently the first to perform the experiment. He reported that of six dogs in which an anastomosis was made between one ureter and a vein, five died on the second postoperative day. One animal lived five days. All refused food, had frequent attacks of vomiting, and the

nonprotein nitrogen of the blood rose to 120 and 300 mg per cent. At necropsy the significant findings were hyperemia and edema of the gastrointestinal mucosa, pericardial and meningeal hemorrhages, early pneumonia, signs of peritoneal irritation, and in two cases pulmonary emboli. He concluded that the kidney must secrete a poison.

In 1927, Galehi and Ito²⁰ working in Brucke's laboratory repeated the experiments with similar results. Of eight dogs with patent unilateral ureter-vein anastomoses, seven died within two days and one survived for five days. The postmortem findings were peritonitis, pneumonia, and pulmonary embolism. These authors also concluded that the kidney secretes a poison in addition to its function of removing waste products from the blood. This poison, they believed, might play a part in the clinical syndrome of uremia.

Hartwich and Hessel²¹ also repeated Brucke's experiment with similar findings. In one group of animals they anastomosed one ureter and the iliac vein, and in another an anastomosis was made between one ureter and the portal vein. Five of the animals in the first group died within 43 hours, one survived 180 hours. The four animals in the second group died within 38 to 73 hours. In each case the blood urea was markedly elevated, the maximum being 453 mg per cent. The postmortem findings were pericardial hemorrhages, fatty infiltration of the liver, acute inflammation of the gastro-intestinal mucosa, and bloody fluid in the peritoneal cavity. These authors likewise concluded that the kidney secretes a poison.

Endeilen, Zukschwert, and Feucht²² preceded the operation of a unilateral ureter-vein anastomosis by a period of eight to ten days of complete obstruction of the ureter to be anastomosed. They then made a side-to-side anastomosis between the distended ureter and either the vena cava or the portal vein. The longest survival after the vena cava anastomosis was ten days, and after the portal vein anastomosis, five days. Jaundice was observed in the animals of the first group but not in those with portal vein anastomoses. An elevation of the blood pressure was reported after each type of operation, but readings were not given. Fatty changes in the liver were not seen. They concluded that the urine from a hydronephrotic kidney was less toxic than that from the normal organ.

Seria,^{23, 24} in 1928, described experiments with four dogs with a unilateral end-to-end anastomosis between the ureteral orifice and the iliac vein, and in which there was evidence at autopsy of free uretero-venous communication. These animals were weak and ate little but did not show the profound post-operative depression described by the previous authors. The blood urea was variable and as a rule did not exceed 120 mg per cent. They were sacrificed after six to 18 days, and at necropsy slight or no hydronephrosis was found on the operated side. There was evidence of inflammation about the anastomoses, and thrombi were present, but water forced into the ureter passed readily into the lumen of the vein. Seria did not believe that his data afforded evidence for the existence of a nephrogenic toxin as postulated by Brucke, but

that the changes in the liver and kidneys described could be attributed to the secretory vicious circle

Lozzi,²⁵ in 1932, reported that dogs, in which a patent uretero-venous anastomosis had been established on one side, regularly died in one to four days. The period of survival was found to be somewhat longer when the urine was drained into the portal vein than when the union was made with the iliac or femoral veins. The nonprotein nitrogen of the blood usually rose to about 110 mg per cent. Fatty infiltration of the liver and degenerative changes in the kidneys were commonly found at autopsy. Although the data presented by Lozzi resemble Brucke's results more closely than those of Serra, Lozzi concluded that it was not necessary to assume the existence of a nephrogenic toxin.

The problem suggested by the reports of Brucke and the others is of such fundamental importance that it seems surprising that it has not aroused more widespread interest. If the experimental data are valid the conclusion that the kidney adds some highly toxic substance to the urine is inescapable. Excision of one kidney or ligation of one ureter does not produce a comparable effect. A somewhat similar situation exists in the case of the biliary secretion. Ligation of the common bile duct may be tolerated fairly well for several weeks or even months, whereas, L. R. Dragstedt and Spurrier²⁶ (1929) found that deviation of the bile into the blood stream by anastomosis of the common bile duct and vena cava or portal vein caused death in about 24 hours.

Experimental Procedure—Healthy, adult male dogs were selected and all operations were performed under ether anesthesia and with aseptic precautions. As in the previous experiments blood pressure determinations were made by inserting a needle connected with a mercury manometer directly into the femoral artery. The right ureter was divided and connected to the right lumbar vein by means of a small glass cannula. The tip of the cannula was allowed to project into the lumen of the vena cava. The posterior parietal peritoneum was closed over the anastomosis. Four successful experiments were accomplished and the results were fairly uniform. Recovery from the operation was prompt and there were no subsequent signs of toxemia. To determine the functional capacity of the kidney on the operated side and the patency of the uretero-venous anastomosis, an intravenous pyelogram was made at various intervals after the operation. The demonstration of contrast medium in the pelvis of the kidney roentgenologically was taken as evidence of the functional integrity of the organ and as an indication that the anastomosis was patent since complete obstruction to a ureter prevents the appearance of the radiopaque dye on the corresponding side.^{27, 28} The findings are summarized in the following protocols.

Dog No. 5—The preoperative blood pressure measured 130 Mm Hg.

Operation—The right ureter was sectioned and connected by a glass cannula with the right lumbar vein. Peritoneum closed over the anastomosis. On the third day the general condition of the dog was good, the blood pressure was 130 Mm Hg, both kidney pelvis were visualized roentgenologically after the intravenous injection of diodrast. On the fourth day the NPN was 27 mg per cent, on the eleventh day 29 mg, and the blood pressure 120 Mm. There were no symptoms of depression. To obtain

additional evidence as to the patency of the anastomosis the right kidney was exposed under ether anesthesia. There was a moderate degree of hydronephrosis. Ten cubic centimeters of a concentrated aqueous solution of methylene blue were injected into the right renal pelvis. Blood samples were drawn from the femoral vein three, five, and ten minutes later and analyzed. The plasma of all three specimens had the greenish tinge which denotes the presence of methylene blue in the blood. The dog was then killed with ether. The region around the anastomosis was covered by a firm, clean scar, there was no evidence of leakage, and the peritoneum was normal. The tip of the cannula was found to project into the lumen of the vein and pressure on the right renal pelvis caused urine to flow freely from the cannula. There was a moderate right hydronephrosis. No fatty infiltration of the liver was found, and microscopic sections of the kidneys were normal.

Dog No. 6—The control blood pressure was 110 Mm Hg.

Operation—The right ureter was connected with the lumbar vein by a glass cannula. Postoperative condition good. N P N on the fourth day was 38 mg per cent. On the eleventh day the blood pressure was 110 Mm Hg, and the pelvis were visualized roentgenologically after intravenous injection of diodrast. The animal was found dead on the thirteenth day. There was a small collection of pus in the region of the anastomosis but no evidence of peritonitis. The tip of the cannula projected into the lumen of the vena cava, there was a moderate right hydronephrosis, and pressure on the right renal pelvis caused urine to flow from the cannula. The lungs were congested, and a small amount of blood tinged fluid was found in the pericardial cavity. The liver and kidneys were normal.

Dog No. 7—The control blood pressure was 130 Mm Hg.

Operation—The right ureter was connected with the lumbar vein by a glass cannula. On the fifth day the blood pressure was 126 Mm, the N P N 29 mg per cent, and both kidney pelvis were visualized roentgenologically after the intravenous injection of diodrast. On the fourteenth day the N P N was 31 mg per cent, and the kidney pelvis were again well visualized. On the thirty seventh day the blood pressure was 120 Mm, the N P N 38 mg per cent, but the kidney pelvis on the side operated upon did not visualize after intravenous injection of diodrast. The animal was in excellent condition and was sacrificed by electrocution. There was a marked right hydronephrosis and a stricture was found in the right ureter near its junction with the cannula. The cannula projected into the lumen of the vena cava and pressure on the right renal pelvis caused a slight flow of clear urine. The liver and kidneys were normal except for a slight dilatation of the tubules of the kidney on the right side.

Dog No. 8—The control blood pressure was 150 Mm Hg.

Operation—The right ureter was connected with the lumbar vein by a glass cannula. On the tenth day the blood pressure was 130 Mm, and the N P N 43 mg per cent. On the eleventh day both kidney pelvis visualized roentgenologically after intravenous injection of diodrast. On the twenty eighth day the blood pressure was 150 Mm, the N P N 44 mg per cent, but the right kidney pelvis did not visualize after intravenous injection of diodrast. The animal was in excellent health and was sacrificed by electrocution. Postmortem examination revealed a marked right hydronephrosis, the anastomosis was good, and on pressure on the right renal pelvis a small blood clot was expressed followed by clear urine. The liver and kidney sections were normal.

Discussion—The results following anastomosis of the urinary bladder with the lower ileum in the present experiments were similar to those reported by Bollman and Mann¹⁸ following implantation of the ureters into the lower intestine. A toxic state was produced characterized by muscular weakness, anorexia, and persistent elevation of the nonprotein nitrogen of the blood. However, vomiting, prostration, and muscular twitchings, such as have been described, accompanying the uremia caused by ligation of the renal arteries or by roentgen-ray damage to the kidneys, were not observed. Degenerative changes in the kidneys, similar to those reported by Hartman²⁹ in the same type of experiment, were found. Hartman attributed these changes to the increase of the nonprotein nitrogen of the blood. The failure of these animals to develop arterial hypertension indicates, either that there is no pressor substance excreted in the urine from normal kidneys, or, if so, it is not absorbed by the intestinal mucosa.

The reports in the literature of profound toxemia, elevation of the nonprotein nitrogen of the blood, rise in arterial blood pressure, and early death with degenerative changes in the liver and kidneys of dogs with unilateral ureter-vein anastomoses, were not confirmed in our experiments. The ani-

imals survived for long periods, in good health, and no changes in the blood pressure or blood chemistry were found. Hydronephrosis on the side operated upon was found in all cases at autopsy, and was evident in the intravenous pyelograms. The cause of this hydronephrosis is not clear. It is not due to complete interference with the passage of urine into the blood stream since diodrast injected intravenously appeared in the pelvis of the kidney as late as 14 days after operation, but not thereafter. Complete ureteral obstruction has been reported to prevent visualization of the corresponding kidney pelvis by this method^{27, 28}. Additional evidence for the patency of the anastomosis was obtained in Dog No. 5 by injecting methylene blue into the right renal pelvis while the animal was under ether anesthesia, then recovering methylene blue from the femoral vein three minutes later. It is probable that the maximum drainage of urine into the blood stream took place during the first few days after the operation, and that this became greatly diminished, or ceased altogether, in the course of several weeks. The failure of these animals, therefore, to display any signs of toxemia or elevation of blood pressure in the period immediately after the operation speaks against the assumption of a specific nephrogenic toxin and indicates that the possible pressor agent in renal hypertension is not a constituent of normal urine.

CONCLUSIONS

(1) Dogs, in which a chronic partial reabsorption of urine has been produced by draining the urine from both kidneys into the terminal ileum, do not exhibit an elevation of arterial blood pressure.

(2) The continued deviation of the urine from one kidney into the blood stream does not produce toxic symptoms or changes in the blood pressure.

(3) These experiments do not support the theory of a specific nephrogenic toxin as suggested by Brucke and others.

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PRIMARY CARCINOMA OF THE URETER

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CLEVELAND, OHIO

FROM THE CLEVELAND CLINIC, CLEVELAND, OHIO

PRIMARY carcinoma of the ureter is a relatively rare malignant disease, although the number of articles on this subject which have appeared in recent years indicates that its occurrence is increasing in frequency or it is being recognized more often than was evident prior to 1920

In 1841, Rayer¹ described the first case of primary carcinoma of the ureter. This was discovered at autopsy and no microscopic description of the tumor was given. Wishing and Blix,² in 1876, cited the first microscopic report of this condition, while Albarran,³ in 1902, established the first verified preoperative diagnosis and in a review of the literature collected ten cases. Meeker and McCaithy,⁴ in 1922, included five cases from the literature that had not previously been noted in collected series and added one of their own, bringing the total to 33. In 1924, Kietschmer⁵ reviewed 34 cases collected from the literature and added one of his own. This number was increased to 50 in 1930 in a publication by Rousselot and Lamon.⁶ Spampinato⁷ collected 88 cases in 1932, but no descriptions of some of the pathologic sections were given in certain instances so all these cases cannot be included in the collected series. Scott,⁸ in 1934, made a comprehensive and critical study of this subject, adding two cases of his own and reviewing 59 reported in the literature. In the same year, Lazarus⁹ collected a series of 68 cases, including three of his own, but he did not include Spampinato's report made two years previously. Cases were also presented during this year by Colston¹⁰ and Harrah,¹¹ and, in 1935, Hunter,¹² and Mathé and Peña¹³ reported similar lesions. In 1936, the collected series was increased by Hosel,¹⁴ Counseller,¹⁵ Gilbert,¹⁶ and Taylor.¹⁷ In a review of the records of the Cleveland Clinic, five cases of primary carcinomata of the ureter have been noted. It is a striking fact that, as refinements have been made in urologic diagnostic methods, the lesion has been observed more frequently. In 1896, Hektoen¹⁸ was able to find in the literature only two references to malignancies in this location.

It is rather difficult to estimate the exact number of cases reported in the literature due to the various terms which have been employed to classify the lesion, and the possibility that the growth may be metastatic or secondary to a tumor outside or elsewhere in the genito-urinary tract. However, as nearly as can be determined, approximately 86 collected cases are available for study at the present time, and the appended five case reports from the Cleveland Clinic series are added.

CASE REPORTS

Case 1—A male, age 63, entered the Clinic in April, 1930, complaining of "kidney trouble" One year previous to our examination, he had first observed the presence of blood in the urine, which was not associated with pain, frequency, or burning The hematuria persisted for several days and then was not noted again until six months later when it recurred, and pain was first experienced in the region of the right kidney At that time, a cystoscopic examination was performed elsewhere and the patient was told the bladder was normal, but that difficulty was encountered in passing a catheter up the right ureter

Three months before he entered the Clinic, gastric upsets occurred frequently, which were characterized by nausea, epigastric distress, and regurgitation of sour food No hematemesis or melena had been noted Examination of the stomach, by the fluoroscope, failed to reveal any gastric or duodenal lesion During the preceding year, since the first appearance of hematuria, the patient had lost 24 pounds in weight

Physical Examination revealed a poorly nourished man with evidence of loss in weight Temperature, 99.4° F, pulse, 76, blood pressure, 170/100 Examination of the heart revealed no abnormality except for frequent extrasystoles The peripheral vessels showed considerable sclerosis Palpation revealed no evidence of disease and there was no tenderness over either kidney or ureter

Laboratory Data—Urinalysis showed 1 plus albumin, 50 to 60 red blood cells, and eight to ten white blood cells per high power field The other laboratory examinations gave essentially normal findings

Initial Roentgenograms revealed no evidence of pathology, and those of the chest and the pelvis were also negative

Cystoscopic Examination revealed coarse trabeculations of the bladder The ureteral orifices were visualized and blood was seen issuing from the right ureteral orifice A ureteral catheter was passed, without obstruction, to the left kidney pelvis, but catheterization of the right ureter met with an obstruction at a point approximately 10 cm from the bladder By means of a Garceau catheter, sodium iodide was injected into the lower end of this ureter and a roentgenogram showed sacculation and obstruction of the ureter at about the brim of the pelvis (Fig 1)

Preoperative Diagnosis—The clinical impression was that the patient had either a primary tumor of the kidney with an implant in the lower ureter or a primary tumor of the ureter itself

Operation—April 29, 1930 A right nephrectomy and ureterectomy was performed The kidney was small but the pelvis was markedly dilated The ureter was dissected down to the bladder and at the point at which the ureter crossed the iliac vessels, a firm tumor mass was found, which measured 4x2x2 cm By careful dissection, this mass was freed from the vessels and the ureter was removed down to within 2 cm of the bladder Convalescence was uneventful and the patient was discharged from the hospital on the twelfth day following operation

Pathologic Examination—*Gross* The specimen consisted of a kidney and 14 cm of the ureter The entire specimen weighed 120 Gm, the kidney showed a large, dilated, extrarenal pelvis and a primary carcinoma of the ureter 12 cm below the kidney The kidney was somewhat smaller than normal, measuring 8.5 cm in length, 5 cm transversely, and 3 cm in thickness Twelve centimeters below the kidney, the ureter enlarged into a nodular mass measuring 4 cm in length and 2.5 cm in diameter This mass was quite firm, immovable and was entirely surrounded by the ureter

Microscopic—A section of the kidney showed sclerosis and hyalinization of the glomeruli in all stages, with only a few scattered glomeruli that were fairly well preserved There was diffuse fibrosis of the cortex and medulla and diffuse and localized lymphocytic infiltration The larger arteries showed a well marked thickening

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of the intima, with degenerative changes and lamination of the elastic coat. The pelvic mucosa showed no evidence of neoplasm.

A section of the ureter above the tumor revealed slight thickening of the wall, hypertrophy of the muscular coat and an atrophic mucosa, dilatation of the submucous blood vessels, and slight inflammatory reaction.

Longitudinal sections through the ureteral tumor showed a papillomatous, epithelial growth involving the mucosa and infiltrating the submucosa, with very little evidence



FIG 1—Case 1. Right ureterogram showing sacculation and obstruction of the lower end of the ureter at about the brim of the pelvis. The filling defect is irregular and suggests tumor of the ureter.

of invasion of the muscular coat (Fig 2). The papillary arrangement was best shown along the free border of the tumor where there were well defined fibrous and well vascularized central areas over the papillomatous growths. These were quite edematous. The tumor cells were fairly uniform in size, type, and staining. They were polyhedral or large and spindle-shaped without glands or pearl formation. Mitotic figures were fairly numerous. A section of the ureter below the tumor showed a small patent lumen lined with normal ureteral mucosa, no thickening of the wall, and no neoplasm. Examination of the peripelvic lymph nodes showed extensive carcinomatous invasion similar

to that described above *Pathologic Diagnosis*—Papillary carcinoma of the ureter
Subsequent Course—The patient died from metastases a few months after leaving the hospital

Case 2—A female, age 58, was seen at the Clinic in December, 1923. Her chief complaint was of pain in the left renal region and in the left hip and thigh. The pain in the kidney region was sharp at times and dull at other periods, and had become more troublesome during the two months previous to examination. She had noted hematuria on several occasions. One sister had died from carcinoma of the breast.

Physical Examination revealed marked tenderness in the suprapubic region, and a cord-like mass of tissue was palpated longitudinally, just lateral to the midline on the left side and spreading out before the level of the umbilicus was reached.

Initial Roentgenograms of the genito-urinary tract did not reveal any suspicious shadows, and a pyelogram of the left side could not be secured.

Laboratory Data—Examination of the urine showed albumin plus 2, and pus plus 2. R B C, 4,500,000, W B C, 11,400.

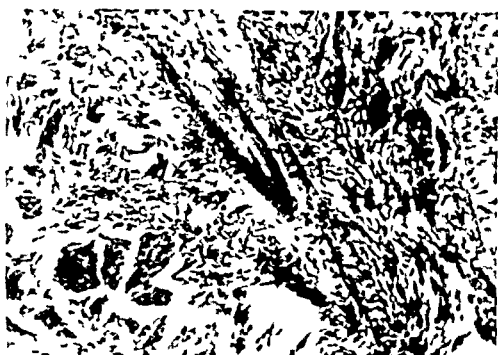


FIG 2—Case 1. Photomicrograph showing papillary carcinoma of the ureter (Original photo X150)

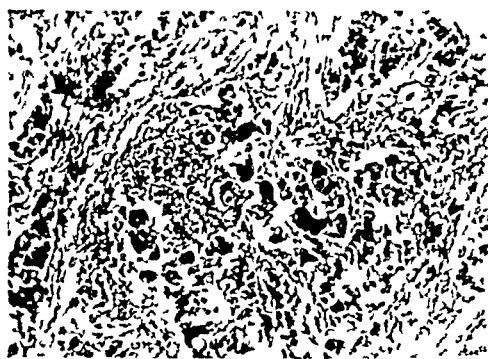


FIG 3—Case 2. Photomicrograph showing papillary carcinoma primary in the ureter (Original photo X150)

Cystoscopic Examinations, of which several were made, revealed a normal-appearing bladder, but an obstruction was encountered about one inch above the ureteral orifice on the left side.

Diagnosis—Papillary carcinoma of the kidney pelvis with implant in the lower ureter or primary carcinoma of the left ureter, nonopaque stone.

Operation—The left ureter was found to be extremely dilated. It was exposed down to the bladder, and at its lower part, approximately one inch above the bladder, there was a hard growth, not attached to the adjacent tissue. The kidney, the ureter, and a small portion of the bladder were removed.

Pathologic Examination—*Gross* Showed that the growth was a papillary carcinoma, primary in the ureter. No tumor was present in the kidney.

Microscopic—Showed a section of fibrous tissue, containing numerous lacunae, in which lay epithelial cells, some in masses and other in papillary rows. The nuclei of these cells varied in size and were very vesicular (Fig 3). *Pathologic Diagnosis* Malignant papilloma of ureter.

Subsequent Course—The patient died, apparently from metastases, two years after operation.

Case 3—A male, age 69, entered the Clinic in April, 1932, complaining of pain in the left lower abdomen, hematuria, and dyspnea. These symptoms had begun about two years previously, during the preceding month gravel had been passed in the urine. Hematuria had first been noticed one year previously, but had not been present constantly. There had been nocturia two to three times for the past two years.

Physical Examination showed a well nourished man, weighing 160 pounds. Temperature 98° F, pulse, 90, blood pressure, 170/100. A loud systolic murmur at the

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apex was transmitted toward the axilla. Palpation revealed no abnormal organs but there was moderate tenderness on deep pressure over the region of the left kidney. The prostate was enlarged, Grade 2, it was firm but not hard or fixed.

Laboratory Data—R B C, 4,680,000, W B C, 9,800, Hb, 89 per cent. The urine contained numerous red blood and a few pus cells. Blood sugar, 110 mg per 100 cc, blood urea, 45 mg per 100 cc.

Initial Roentgenograms revealed no abnormal findings.

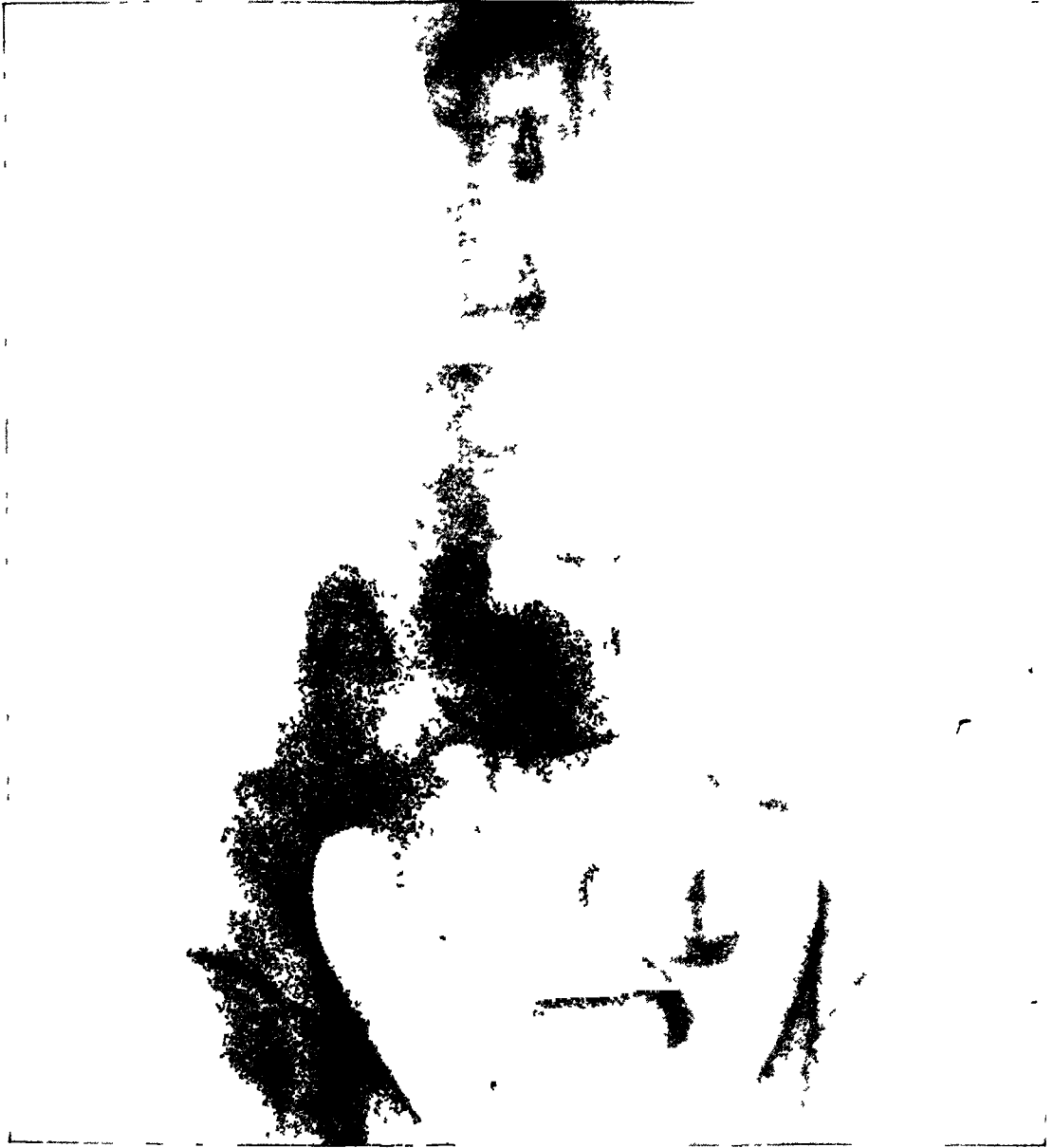


FIG 4—Case 3. Intravenous urogram showing no evidence of visualization of the left kidney and ureter, with a large diverticulum of the bladder. The total function was good.

Cystoscopic Examination revealed a large amount of bloody urine in the bladder. In the region of the left ureteral orifice there was a large diverticulum. The ureteral orifice could not be visualized and blood could be seen spurting out of the diverticulum.

An *Intravenous Urogram* showed the right kidney and ureter to be normal (Fig 4). The left kidney pelvis and the ureter were not visualized.

Diagnosis—Obstruction of left ureter due to tumor or nonopaque calculus.

Operation—A tumor was found in the left lower ureter about one inch above the

ureteral orifice which emptied into the diverticulum. The lower ureter and the diverticulum were removed and the ureter reimplanted into the bladder. The patient died from pulmonary complications three days later.

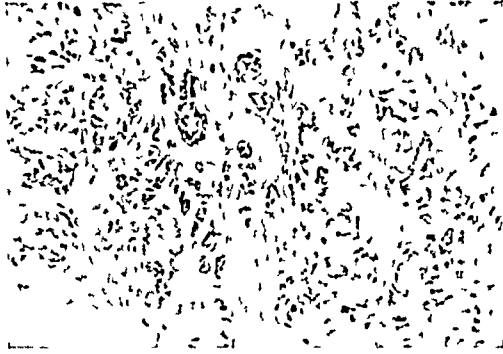


FIG 5—Case 3. Photomicrograph showing primary carcinoma of the ureter. (Original photo $\times 150$)

Pathologic Examination—Microscopic

Section of the tumor showed diffuse infiltration of the coats of the ureter by small and large solid masses of epithelial cells showing numerous mitotic figures and irregular nuclear divisions (Fig 5). The neoplastic infiltration extended from the mucous membrane, which was partially destroyed and replaced, to the adventitia in some areas. In the outer coat, clumps of tumor cells were present in the lymphatics.

Pathologic Diagnosis—Carcinoma of the left ureter, diverticulum of the bladder.

Case 4—A female, age 55, came to the Clinic in July, 1933, complaining chiefly



FIG 6—Case 4. Intravenous urogram showing visualization of the left kidney which appears to be normal. The right kidney and ureter were not visualized.

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of pain in the right renal area, hematuria and burning on urination which had been present for about two years. The burning occurred at the end of urination, but the urine itself was red in color. During the preceding few weeks, nocturia two or three times had been present.

Physical Examination revealed a well nourished woman, weighing 151 pounds. Pulse, 90, temperature, 98° F, blood pressure, 140/85. No abdominal organs were palpable and no tenderness was elicited over either kidney. On vaginal examination, a small, hard mass was palpable to the right of the cervix. This mass felt like a calculus in the lower right ureter.

Laboratory Data—R B C, 4,000,000, W B C, 8,200, Hb, 88 per cent. Urinalysis showed faint traces of albumin, numerous pus cells, and a few red blood cells. The Wassermann reaction was negative. Blood urea, 36 mg per 100 cc.

Initial Roentgenogram showed no abnormal findings.

Cystoscopic Examination revealed a tumor about the size of a hulled hickory nut protruding from the right ureteral orifice. The tumor was irregular and quite vascular, and was believed to be secondary to a tumor of the right kidney pelvis.

Intravenous Urograms visualized the left kidney, which appeared normal (Fig 6). The right kidney and ureter were not visualized.

Diagnosis—Primary carcinoma of the right ureter or implant from carcinoma of right kidney pelvis.

Operation—October, 1934. The right kidney and ureter were removed.

Pathologic Examination—*Microscopic*. Revealed a squamous cell carcinoma of the right ureter. Section through the ureter and tumor mass showed some areas of normal mucosa, but in other areas the mucosa was replaced by tumor tissue, which consisted of solid masses of epithelial cells which did not form glands or pearls. There was extensive infiltration by tumor cells, large areas of necrosis in the tumor, and a mild inflammatory reaction (Fig 7). *Pathologic Diagnosis*—Squamous cell carcinoma of the ureter.



FIG 7—Case 4. Photomicrograph showing squamous cell carcinoma of the ureter (Original photo $\times 150$).

Subsequent Course—The patient returned to the Clinic five months later, February, 1935, complaining of pelvic pain, and roentgenotherapy was instituted. Her condition at that time was critical, no further word, however, has been heard from her.

Case 5—A male, age 75, came to the Clinic, January 25, 1935, complaining of difficulty in urination, pain in the lower back, and vague pain in the region of the left kidney. These symptoms had been present for about a year. Three days before admission, bright red blood had been passed in the urine. Cystoscopic examination had been performed elsewhere, and the patient had been told that there was a mass in the lower left wall of the bladder. The patient said he had lost approximately ten pounds in weight during the preceding year.

Physical Examination revealed a fairly well nourished man weighing 160 pounds. Temperature, 98.6° F, pulse, 70, blood pressure, 150/90. The examination revealed no abnormalities aside from a Grade 2 enlargement of the prostate.

Laboratory Data—R B C, 5,129,000, W B C, 11,000, Hb, 81 per cent. The urine contained traces of albumin, 2 plus white blood cells, and 4 plus red blood cells. Blood urea, 45 mg. Wassermann reaction, negative.

Initial Roentgenograms showed moderate hypertrophic changes in the lumbar spine.

Cystoscopic Examination—Two hundred cubic centimeters of residual urine were

withdrawn. The bladder was carefully examined and no tumor was observed. There was a median lobe elevation of the posterior commissural type and only slight lateral lobe intrusion. On the left side, the catheter passed up the ureter about 6 cm, where it met a definite obstruction. Some resistance to the passage of the catheter was also encountered on the right side, this caused severe pain. On removing the catheters, a considerable quantity of bright red blood came from the left ureteral orifice.

Röntgenologic Examination—A pyelogram of the right kidney showed a normal



FIG 8—Case 5. Left ureterogram showing obstruction of the lower left ureter and dilatation at the upper portion of this obstruction. There is some irregularity suggesting tumor of the ureter.

pelvis. The left lower ureter showed an obstruction and little dilatation at the upper portion of this obstruction. There was some irregularity suggesting a tumor of the ureter (Fig 8).

Diagnosis—Carcinoma of the left ureter.

Operation—June 29, 1935. A nephro-ureterectomy was performed. At about the junction of the lower and middle thirds of the ureter, a spongy mass was encountered. This was not adherent to adjacent structures, was soft in consistency, and measured 3x1.5 cm, the ureter being dilated above the mass and appearing normal below it.

Pathologic Examination—Gross The specimen consisted of a kidney and ureter weighing 180 Gm. The kidney measured 11.5×5.5×4 cm. It was slightly enlarged and covered by a thin capsule which stripped easily, leaving a smooth surface, except for the presence of two cysts on the posterior surface. Vertical section through the kidney showed slight dilatation of the pelves and calices, considerable peripelvic fat, and no calculi or papillomatous growths.

The renal parenchyma was pale and cloudy. There were no abscesses or tumor masses in the kidney. The ureter was moderately dilated and the wall was thin. There was a tumor mass in the ureter, with its center 12 cm. below the ureteropelvic junction. The tumor was 3 cm. in length and involved the entire ureteral wall. The surface of the tumor was granular and somewhat papillary.

Microscopic Examination of a section of the ureter through the tumor showed a papillary carcinomatous growth with extensive ulceration on the surface, infiltrating all the coats, perforating the muscular coat, and extending into the adventitia (Fig. 9). The tumor was made up of quite small, deeply staining cells of uniform type in which mitotic figures were fairly numerous. *Pathologic Diagnosis*—Primary papillary carcinoma of the left ureter.

Subsequent Course—The patient died from pneumonia four days after operation. Postmortem examination revealed no evidence of metastases.



FIG. 9—Case 5. Photomicrograph showing primary papillary carcinoma of the left ureter. (Original photo $\times 150$.)

Age Incidence—The ages of the patients in this series of cases of primary carcinoma of the ureter were 63, 58, 69, 55, and 70 years, respectively. The average age was 63 years, this being slightly higher than that reported in the literature. In the 60 cases reviewed by Scott,⁸ the ages of the patients averaged 55.7 years, the youngest patient being age 33, the oldest, 89. From a review of the literature, the disease is noted to occur with about equal frequency in the fifth, sixth, and seventh decades of life.

Sex Distribution—Carcinoma of the ureter occurs with about equal frequency in both sexes. In this series, three patients were men and two were women. The ratio in the 68 cases reviewed by Lazarus⁹ was 32 women and 36 men.

Location of Growth—The right and left ureters are involved in about the same frequency. In this series, the right ureter was the site of the malignant lesion in two instances and the left ureter in three. Scott⁸ listed the site of the lesion in 61 cases, stating that the right ureter was involved in 34 and the left ureter in 27 cases. In Lazarus⁹ collected series, 32 occurred in the right ureter and 33 in the left.

The upper third of the ureter is a rather uncommon site for this malignant lesion. In our series, the tumor was in the lower one-third of the ureter in three cases and 12 cm. below the ureteropelvic junction in two cases. In the series reviewed by Scott, the lower one-third of the ureter was involved in 57 per cent of the cases, and in only 11 of 61 cases was the upper one-third of the ureter the primary site of the tumor.

Symptoms—There are no symptoms sufficiently characteristic to suggest carcinoma of the ureter, but in a given case where the triad of symptoms is present—pain, hematuria, and tumor—its possibility must be considered. All the patients whose cases are presented here had had at least two of these symptoms. In one case all three symptoms were present, the tumor having been felt through the vagina as a hard mass in the region of the lower end of the right ureter. However, when such a tumor is palpable, the possibility of a calculus in the lower ureter or tuberculous involvement of the ureter must be considered.

Pain—Pain occurs in from 60 to 65 per cent of the cases. Stewart¹⁰ states that three types of pain may occur: (1) Attacks of acute colic due to the passage of clots, (2) more constant pain due to ureteral obstruction, producing a dilatation of the renal pelvis, (3) severe or lancinating pain in the lower lumbar and sacral regions caused by infiltration of the adjacent tissue by the malignant tumor itself. In the latter group the lesion is no longer confined to the ureter and the prognosis is, therefore, more grave.

The patients in our series complained of pain in the kidney region, which was found to be due to a hydronephrosis caused by partial obstruction of the ureter.

Hematuria is probably the most important symptom of carcinoma of the ureter. It was present in all five patients seen at the Cleveland Clinic, and it occurred in 72 per cent of the series reviewed by Scott. Although the bleeding may be constant, intervals of freedom from gross hematuria may occur. The presence of clots of blood may also be noted by the patient. The bleeding was more pronounced in our series when the lesion was a papillary carcinoma, and less evident in the patient with the squamous cell carcinoma of the ureter.

Tumor—In about 45 per cent of the cases recorded in the literature, a palpable mass was present in the renal area. The most frequent cause of the mass was a hydronephrosis of the kidney. In some of the cases, the growth in the ureter may be detected by abdominal palpation (Case 2 of this series). Similarly the tumor may be palpable upon vaginal examination, as occurred in Case 4.

Coexisting symptoms not directly referable to the malignant growth itself may be present. In one patient, symptoms of obstruction of the vesical neck due to prostatic hypertrophy were present. Dyspnea, frequency, loss of weight, or passage of gravel may be additional symptoms.

Diagnosis—The final diagnosis is arrived at by careful urologic study. Of especial value are the findings of cystoscopic and the roentgenologic examinations. In some instances, it is impossible to make a definite diagnosis, and in 62 per cent of the reviewed series reported by Lazarus,⁹ the diagnosis of ureteral tumor was not even suspected before operation or necropsy.

Cystoscopic examination may show blood coming from the ureteral orifice or, after the passage of a ureteral catheter, profuse bleeding may follow its

removal This provocative type of bleeding was described by Chevassu and Mock,²⁰ in 1912 However, it may also occur following vaginal examination in cases where the tumor occupies a position low in the ureter

Small tumors, implants from the parent tumor in the ureter, may be present about the ureteral orifice, or the small tumor may actually protrude from the orifice itself The possibility of a tumor of the renal pelvis with implantation of a secondary tumor in the lower ureter must be considered in these cases If retrograde pyelography or an intravenous urogram shows absence of a filling defect in the kidney pelvis, the lesion is probably due to a primary tumor of the ureter

A persistent filling defect in the ureter, as visualized by a pyelo-ureterogram, is probably the most pathognomonic of all findings Dilatation of the ureter above the filling defect with a hydronephrosis and absence of a filling defect in the kidney pelvis, form a strong inference that the lesion is primary in the ureter This may be simulated by nonopaque stones or extraluminal pressure upon the ureter, but the differentiation is usually possible Intravenous urography is valuable in instances in which the obstruction prevents the passage of a ureteral catheter to the kidney pelvis, and it is also of value in determining if the obstruction is due to a stricture of the ureter A number of the recent reports in the literature include those in which a correct diagnosis was established before operation These diagnoses were largely made by correctly interpreting the roentgenograms Harish¹¹ has recently presented an excellent discussion of these roentgenologic findings, while other authors who have established an accurate preoperative diagnosis of carcinoma of the ureter and have discussed the subject include Davis and Sachs,²¹ Playe,²² and Gruneberg²³ Taylor¹⁷ also presented two cases, in the first of which a probable diagnosis was made because of the presence of a tumor in the ureteral orifice, and in the second case it was made because of a filling defect shown on the ureterogram

Thus by careful physical examination and the employment of cystoscopic examination, retrograde pyelography, and intravenous urography, a diagnosis may often be established prior to operation

Treatment—The operation of choice is complete nephro-ureterectomy and removal of a small cuff of bladder about the ureteral orifice Sometimes it is necessary to remove a larger portion of the bladder if the tumor occupies a position in the lower ureter in close proximity to the bladder

At times a radical procedure may not be justifiable, due to the poor general condition of the patient, or in some instances the function of the opposite kidney may be so impaired that to sacrifice the kidney on the involved side would subject the patient to considerable postoperative risk In such instances, the involved ureter may be removed first, followed later by a nephrectomy, if the other kidney functions well, or by a nephrostomy if indicated by poor function of the other kidney

When the tumor is in the upper or middle third of the ureter, I believe

the latter should be removed in its entirety, as implants may be present in the lower ureter. While some authors have recommended less radical procedures for tumors in this situation, I believe they are rarely indicated. Each patient must be individualized and the procedure instituted which is compatible with the preoperative study of the renal function and the general condition of the patient.

Postoperative roentgenotherapy is administered for, even at the time of operation, it may be impossible to ascertain definitely if the involvement of the adjacent lymphatics has occurred.

Results—Carcinoma of the ureter is most discouraging from the standpoints of prognosis and prospects of a cure. The postoperative mortality is high, approximately 25 per cent in the collected series. Scott⁸ has emphasized this and pointed out the high incidence of shock following nephroureterectomy. Two of the five patients in our series died from pulmonary complications within a few days after operation. One patient had a recurrence of the growth, and a mass was palpable in the left inguinal region seven months later. The patient died from metastases one year and four months after surgical intervention.

The fourth patient returned in poor physical condition, several months after nephroureterectomy (Case 1). Metastases were present. No further reports could be secured from follow-up letters after this visit. The patient probably died from metastases. The fifth patient died from metastases within one year after operation (Case 2).

A large majority of patients with carcinoma of the ureter die within two years after surgical removal of the kidney and ureter. In most cases, the lesion is well advanced when the patient seeks surgical relief, and regional metastases, or recurrences following operative intervention, develop in most instances.

Scott, in a careful follow-up study of the cases reported in the literature, found only two patients alive and well more than five years after operation. One patient reported by Kjaft,²⁴ in 1922, was well 11 years following nephroureterectomy for a papillary growth of the ureter. A patient reported by Crance and Knickerbocker²⁵ was still living eight years after nephroureterectomy for an epithelioma of the lower portion of the right ureter.

Hunter,²⁶ in his discussion of McCown's paper, published in 1930, stated he had operated upon one patient with carcinoma of the lower ureter, removing the involved portion, and the patient was well and showed no signs of recurrence four years later.

As stated previously, all the patients operated upon in this series died within a period of two and one-half years following operation.

Pathology—The most frequent type of primary carcinoma occurring in the ureter is papillary carcinoma. In this series three tumors were classified as papillary carcinomata, one as carcinoma, and one as squamous cell carcinoma. About 40 per cent of the cases reported in the literature are grouped under the heading of papillary carcinomata. In the collected series reported

by Scott, 36 of the 61 cases were reported to have been of this type. The nonpapillary group have been classified as squamous cell carcinoma, scirrhous and encephaloid carcinoma, medullary carcinoma, carcinoma solidum, and various other groupings.

Metastases are frequently observed, and involvement of the regional lymph nodes was noted at the time of operation, or at necropsy following operation, in 48 per cent of cases. While it has been stated that metastases may occur early, it must also be recalled that the lesion may be present for a considerable period of time before a diagnosis is established and operative intervention instituted. Metastases may occur by lymphatic extension or by the blood stream, the retroperitoneal lymphatics being the most frequent avenue of extension. Scott illustrated a case in which a small thrombus mass of tumor cells was found in the vena cava.

Thus, although at operation the tumor seems confined to the ureter, the possibility of metastases must be considered and the prognosis guarded.

CONCLUSIONS

(1) Five cases of primary carcinoma of the ureter, verified by operation and pathologic study, are reported.

(2) Carcinoma of the ureter, although rare, is being observed and reported with increasing frequency.

(3) The prognosis in carcinoma of the ureter is grave.

(4) Diagnosis is accomplished by cystoscopic examination and roentgenologic study.

(5) The treatment of choice is nephro-ureterectomy followed by roentgenotherapy.

(6) Papillary carcinoma is the type of growth most frequently encountered in the ureter.

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THE FATE OF TENDON, FASCIA AND ELASTIC CONNECTIVE TISSUE TRANSPLANTED INTO BONE*

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CONNECTIVE tissue in an altered environment may undergo metaplasia. It was demonstrated by Neuhof¹ that if a defect in the urinary bladder of the dog is patched with fascia and by Huggins² that if urinary bladder epithelium is transplanted to fascia, the urinary epithelium proliferates at the cut margins and stimulates bone formation on the part of the fascia. Buiman and Umansky,³ also, have demonstrated in rabbits that periosteum transplanted about tendon forms a scar which undergoes partial ossification. This raises the question whether connective tissues transplanted into bone may not undergo ossification in this abnormal environment.

It is also of practical importance to know the method of anchorage of tendon and fascia when they are inserted into bone in operative procedures. Firm anchorage is known to follow such implantations but Gallie⁴ has also reported some failures, both in human cases and in experimental animals.

Experimental Procedures—Three types of tissue—tendon, fascia lata, or white fibrous connective tissue and ligamentum nuchae or elastic connective tissue—were transplanted into bone by the following technic. Under aseptic conditions, either the tibia in rabbits or the femur in dogs was exposed, and using a drill, a canal was made through the bone, the soft tissue transplant pulled through and its ends approximated and sutured together with fine silk. In a few cases fascia was inserted into the medullary cavity through a window in the cortex. The animals were then sacrificed at intervals ranging from 60 to 391 days in groups of three so that comparative studies could be made of the various soft tissues.

Experiment No 219—Fascial Transplant (dog)—duration 60 days. The section is cut so as to include both drill-holes and show the fascial transplant passing transversely completely across the femur at this level. A narrow trabeculum of newly formed bone lies in contact with both surfaces of the fascia, separating it from the medullary cavity except in the very center. Here there are interruptions in the bony continuity and marrow tissues streaming through in places and invading the fascia. There is thus formed a highly cellular strip about the periphery with round cells, immature fibroblasts and blood vessels present in large numbers. The central portion of the fascia is markedly hyalinized and only occasional long thin nuclei are seen.

Where the fascia passes through one of the drill-holes, osteoblasts are seen in-

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vading the fascia and replacing it with bone, while at the other defect of the cortex a thin layer of bone covers the ends transversely and there is a thick layer of richly cellular fibrous tissue between this and the remnant of old fascia at the central portion (Fig 1)

Experiment No 279—*Tendon Transplant* (rabbit)—duration 54 days The tendon cut in cross-section is seen lying in the medullary cavity bordered on one side by a semicircular layer of new bone and on the other side by marrow tissue. In a part of the portion bordered by marrow there is a richly cellular layer, mostly fibroblasts which are invading and replacing the fascia. The central portion of the tendon is mostly hyalinized and relatively acellular. There is no metaplasia present and replacement of the tendon by bone is minimal.

Experiment No 424—*Ligamentum Nuchae* (dog)—duration 63 days There are five sections which include both cortical defects and show the ligamentum nuchae transplant at various levels and extending transversely across the femur. Newly formed bone covers the surface of the transplant throughout. The regions of contact between ligament and bone in some places have osteoblasts which are invading and replacing the ligament with new bone, in other places flame-like streaks of new bone extended out into the ligament and are converting it into new bone by a process of metaplasia (Fig 2). Centrally the ligament is densely hyalinized. At the point where the ligament passes through the cortex it has been largely ossified.

Experiment No 281—*Tendon Transplant* (rabbit)—duration 86 days The section passes obliquely through one drill-hole. This is partly occupied by tendon which is cut obliquely. Externally it reaches a short distance beyond the cortex and internally it ends just short of the medullary canal. Marrow tissues protrude from the medulla to fill the inner portion of the drill-hole. A layer of new bone has formed from the wall on either side to fill about one-half the diameter of the drill-hole. The rest is occupied by tendon. The peripheral portion of the tendon consists of a relatively acellular eosin staining fibrillar tissue. The central portion contains a streak of new bone the lamellae of which run longitudinally and contain cells arranged longitudinally in rows (Fig 3). At one end and along the sides this bone island seems to be growing by the formation of new bone from osteoblasts. In the center is a marrow space occupied by fibroblasts and a few hemopoietic cells.

This atypical bone has formed as a result of metaplasia of this tendon and has no connection with the bone formed from the cortex about the margins of the drill-hole. It is analogous to tendon ossification seen regularly in the feet of fowl and sometimes in man.

Experiment No 523—*Tendon Transplant* (dog)—duration 115 days The tendon is hyalinized centrally (Fig 4). There is a hyperplasia of the osteoblasts along the border of contact of cortical bone with tendon as well as considerable ossification of the richly cellular connective tissue along this junction. Where the tendon lies in the medullary portion, there is no new bone formation except along the border of contact of tendon with encompassing bone. Here there is seen a richly cellular tissue but only a very slight amount of ossification.

Experiment No 275—*Tendon Transplant* (rabbit)—duration 102 days The central portion of the tendon is densely hyalinized. Peripherally there is invasion by a richly cellular connective tissue with many round cells and a few giant cells. Focally, regions of new bone formation extend out from the wall, and, encroaching upon the tendon, encapsulate and replace portions of it. At one perforation in the cortex the tendon is largely replaced by new bone and that which remains appears alive peripherally and hyalinized centrally.

Experiment No 62—*Fascial Transplant* (dog)—duration 124 days The transplant lies dormant in the medullary cavity and is surrounded by a layer of new bone. It is densely hyalinized except for a narrow strip about the periphery. In some places osteoblasts may be seen invading and replacing the tendon with new bone. A piece of

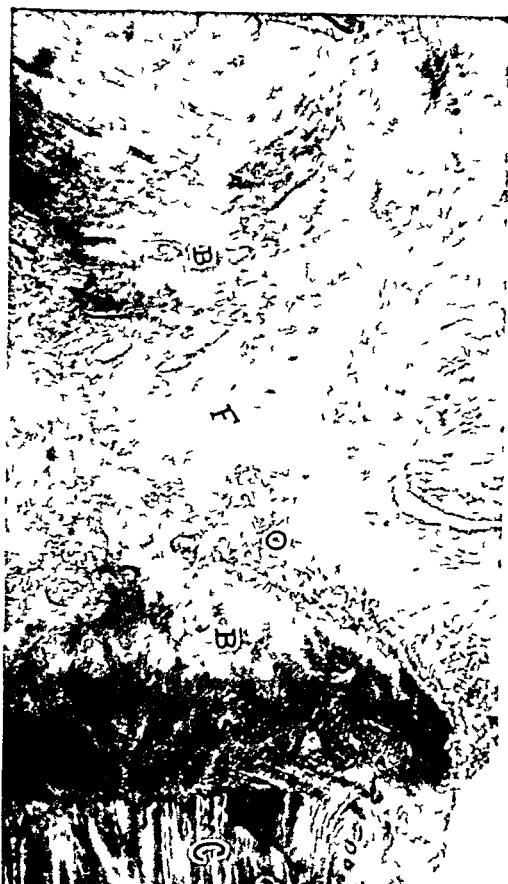


Fig. 1—Experiment No. 219. Fascial transplant of 60 days' duration seen passing through cortex of femur of a dog. The cortex (C) borders the defect created by the drill and regionally is devoid of cells. The fascial transplant (F) is being invaded from both sides by osteoblasts and vascularized connective tissue. A large portion of the transplant is already ossified (B).



Fig. 2—Experiment No. 424. Elastic connective tissue transplant to femur of 63 days' duration. The central portion of the elastic connective tissue (L) is relatively acellular, the periphery (B) contains many cells by virtue of its invasion by a highly vascularized connective tissue. Ossification of the invading transplant is seen at (O) and is the work of the many osteoblasts seen in these regions.



Fig. 3—Experiment No. 281. Tendon transplant into bone of 86 days' duration. The acellular and hyalinized tendon (T) is seen lying outside the cortex. In its center it (B) there is seen an island of atypical bone. Note its lamellar and cells are in longitudinal rows and roughly parallel the course of the fibers of the tendon. In the center of this bony island is some marrow tissue. The cortex of the femur (C) in no way contacts the atypical bony island of the tendon. This is a true multiphasic.



Fig. 4—Experiment No. 523. Tendon transplant to femur of dog of 115 days' duration. The section shows the invasion of the acellular tendon transplant (T) by osteoblasts along the periphery (P) and incorporation of the tendon into the bone by ossification seen well at (O).



FIG 5—Experiment No. 62 Fascial transplant into femur of dog of 124 days' duration. The section shows the line of junction of cortical bone (B) and fascial transplant (F) with collagen fibers (C) resembling Sharpey's fibers passing from unossified into ossified tissues where they are transformed into bone by metaplasia. Under high power in the region (S) one can readily identify the remnants of a silk suture attesting the complete metaplasia of the fascial which originally accompanied it.



FIG 6—Experiment No. 109 Elastic tissue transplant (ligamentum nuchae) into femur of dog of 131 days' duration. Elastic connective tissue (L) are seen pressing from ligamentum nuchae (L) into ossified tissue (B). This is a metaplasia of elastic connective tissue into bone and demonstrates another method of ossification and anchoring of soft tissue by incorporation into bone.



FIG 7—Experiment No. 102 (Ligamentum Nuchae.) Elastic connective tissue transplanted into femur of dog of 291 days' duration. The section shows the response of medullary tissues to soft tissue transplants. The elastic connective tissue (L) is only partially surrounded by a thin trabeculum of bone (B). There is no evidence of ossification or attempt at incorporation of the transplant by the medullary tissue.

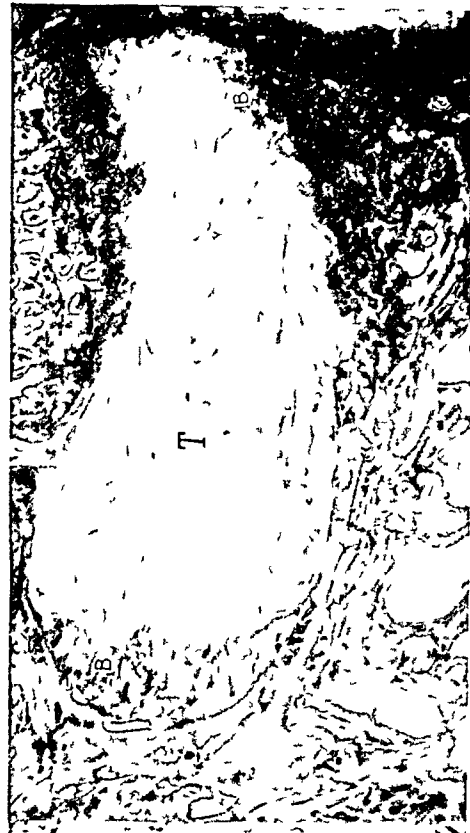


FIG 8—Experiment No. 715 Tendon transplant into cancellous bone of dog of seven months' duration. This section demonstrates that cancellous bone reacts like cortical bone toward soft tissue transplants. The tendon (T) is seen lying completely surrounded by cancellous bone. Ossification of the tendon by osteoblasts is seen in the region (O).

silk entirely surrounded by new bone attests the complete ossification of the tendon which accompanied it (Fig 5) Near by several tongues of collagen fibers extend into the bone, resembling Sharpey's fibers, and appear to be undergoing metaplasia into bone

Experiment No 109—*Ligamentum Nuchae* (dog)—duration 131 days Four sections show the ligament cut in cross-section and lying at a level where cortex and medullary cavity meet The transplant is completely surrounded by new bone and for the most part appears to be lying dormant From one side, however, there is a flame-like extension of ossification from the cortex into the ligament in the direction of the latter's fibers, and collagen fibers are seen passing from the nonossified into ossified regions where they are undergoing metaplasia into bone (Fig 6)

Experiment No 33—*Fascial Transplant* (dog)—duration 133 days One section shows the fascial transplant lying in the medullary canal surrounded by a thin shell of new bone Peripherally, marrow tissues stream through interruptions in the bony shell and form a richly cellular and vascular layer, centrally the transplant is densely hyalinized

The other sections are at a level where the window in the cortex remains open Strands of silk suture entirely surrounded by new bone attest the complete replacement of the accompanying fascia by bone Focally, about the periphery of the transplant there are regions of active replacement of fascia by bone No metaplasia is present in the medullary area In the cortical portion the transplant has been completely replaced by bone It is, therefore, impossible to say whether or not there was any metaplasia in this region

Experiment No 151—*Ligamentum Nuchae* (dog)—duration 158 days The transplant is largely hyalinized with only widely separated nuclei present In the medullary region it lies dormant, surrounded by a shell of new bone, with only focal regions where osteoblasts may be seen invading and replacing it In the cortical area large portions of the ligament have been completely replaced by bone, only isolated individual strands of silk remaining In places collagen fibers extend from the nonossified into the ossified areas and flame-like projections of bone extend out into the ligament and appear to be transforming it into bone This latter is again an example of metaplasia of ligamentum nuchae into bone

Experiment No 102—*Ligamentum Nuchae* (dog)—duration 291 days The cortical defect is practically closed In the medullary cavity the hyalinized transplant appears to be lying dormant and is only partially covered by a thin shell of bone (Fig 7) No new bone formation is seen

Experiment No 461—*Tendon Transplant* (dog)—duration 391 days A transplantation of the biceps tendon through the humeral head was performed The tendon has been almost completely replaced by a richly cellular and vascular connective tissue Throughout one sees focal areas of replacement of this tissue by new bone There is no metaplasia

Experiment No 715—*Tendon Transplant into Cancellous Bone* (dog)—duration seven months The tendon is completely surrounded by bone The junction of tendon with bone blends gradually one into the other through a richly cellular connective tissue which is being ossified by osteoblasts invading from the periphery (Fig 8)

DISCUSSION—Connective tissue of three types was transplanted into drill-holes in the bones of 67 animals, 13 of which experiments are herewith reported

The trauma of the drill created conditions locally in the bone which closely simulated those present in a fracture except that its supporting function was not reduced There was a hemorrhage with organization of the clot by fibroblasts and the formation of osteoblasts which in turn formed a bony wall about the transplant

Due to a lack of nourishment the transplants routinely underwent more or less retrogressive changes. These were characterized by an increase in the relative amount of collagen fibers present and a decrease in the number as well as the staining quality of the cells. The cells appear to be in a resting or "hibernating" state. Peripherally where the blood supply had been reestablished there was a densely cellular layer. Most of these cells had invaded the transplant along with the blood vessels from the marrow but many were undoubtedly revived, so-called "hibernating" cells described above.

There was a marked difference in the reaction of the medullary tissues, as compared with the cortical, toward the transplant. In the medullary region the transplant, walled off from the marrow by a thin bony septum, universally appeared to be lying dormant (Fig 7). In the cortical region the reaction was characterized by an ossification of the transplant. The ossification of all three types of soft tissue transplants was by two entirely different methods. The one was an invasion of the transplant by osteoblasts which formed bone and then replaced the soft tissue (Figs 1, 2 and 4), the other appeared to be a true metaplasia (Figs 2, 5 and 6).

CONCLUSIONS

(1) Ligamentum nuchae, tendons and fascia lata of both dogs and rabbits when transplanted into bone suffered nutritional disturbances but remained viable and tended slowly to become ossified.

(2) The ossification of the transplant was most marked in the cortical area, being only minimal in the medullary portion.

(3) Ossification of the soft tissue transplants occurred in two ways (1) Replacement by invading osteoblasts which formed bone, and (2) by metaplasia.

(4) The firm anchorage obtained by passing the tendon through drill-holes in bones is due to their gradual ossification and incorporation in the bone.

(5) Lack of function had no demonstrable effect on the above changes.

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AN EVALUATION OF EXCISION IN THE TREATMENT OF UNUNITED FRACTURE OF THE CARPAL SCAPHOID (NAVICULAR) BONE

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THE progress in the successful treatment of fracture of the carpal scaphoid (navicular) bone during the past decade has been unique. Where nonunion was formerly invariably anticipated, union is now obtained by proper conservative measures in a high percentage of cases, largely due to the teachings of Berlin,¹ Soto-Hall and Haldeman,² Bohler,³ Watson-Jones⁴ and others. However, despite the success of these altered concepts, a small but definite percentage of intra-articular fractures of the carpal scaphoid, through or proximal to the waist, fail to unite. In addition, because many "sprained wrists" are inadequately investigated, and because roentgenographic findings in recent cases are often indefinite or absent, many fractured scaphoids remain undiagnosed until irreparable damage has occurred.

The factors that lead to nonunion are probably a combination of incomplete reduction, inadequate fixation and disturbed blood supply. Yet, far too often, nonunion is seen to occur despite accurate and prolonged immobilization, while, on occasion, union will take place in the presence of considerable aseptic necrosis of the bony fragments. The studies of Johnson⁵ and Speed⁶ contradict the suspected lytic effect of synovial fluid as a cause of nonunion in these intra-articular fractures, while open reductions have repeatedly failed to substantiate the contention that the dorsal capsule becomes interposed between the fragments.

These patients evidence painful disability of the affected wrist, tenderness in the region of the scaphoid, restriction of motion, especially of dorsiflexion and radial deviation, weakness of the grip and atrophy of the forearm musculature.

Roentgenologic studies reveal varying degrees of sclerosis and porosis, fragmentation and vacuolization of the fracture fragments. The site of pseudarthrosis is accentuated by sclerosis of the adjacent bony margins and surrounding osteitis, changes formerly ascribed by Preiser⁷ to a distinct disease entity complicated by fracture, but now considered as bony changes subsequent to trauma and fracture. New bone (exostosis) formation, especially at the lower articular radial surface, appears in one to two years.

Such definite roentgenographic findings, in the presence of positive clinical signs and a traumatic history, serve to exclude bipartite scaphoid, an infrequent developmental anomaly reported by several authors,⁸ and seen by us once in 200 anatomic specimens.

Cases with delayed or early nonunion have been successfully treated by Bohler with prolonged fixation for six to eight months with nonpadded plaster bandages extending from the base of the fingers to the upper forearm, including the thumb, and with the wrist hyperextended and in ulnar deviation.

Reports of satisfactory union in neglected, ununited cases have followed the use of subcutaneous, multiple drillings across the fracture site under fluoroscopic control, as advocated by Schnek⁹ of Bohler's Clinic, employing Beck's method of drilling, and by Soto-Hall and Haldeman,² who recommend this drilling procedure after exposure and curettage of the fracture site.

The use of an autogenous bone graft or peg, as utilized independently by Adams and Leonard¹⁰ and Smith,¹¹ has been popularized by Murray,¹² Burnett¹³ and others. Murray claims to have obtained osseous union in 16 cases of delayed or ununited carpal scaphoid fracture while Burnett, reporting satisfactory results, admits obvious fibrous union (roentgenographically) in most of his cases.

The increasing literature on these newer forms of therapy has served to place the operative procedure of total excision in dispute. Excision, notwithstanding, has a very definite place, for it is still the operation of choice in (1) Fractures that are irreducible even following open reduction, (2) badly comminuted fractures of the scaphoid, especially those associated with other injuries of the wrist, as a dislocated semilunar bone, and (3) neglected cases of nonunion with marked and irreparable degeneration of the bony fragments.

In addition, we have the temerity, although quite cognizant of the value of the drilling and bone-graft procedures, to recommend total excision in cases that show obvious nonunion and persistent disability, following a fair, but not too prolonged conservative regimen, where the economic status of the patient, his livelihood, and the medico-legal aspects of his case, require early return to work. Early excision will result in a normally functioning and painless wrist, with little or no deformity and the element of possible failure that accompanies prolonged conservative treatment and either the drilling or bone-graft operations, is obviated.

If total excision is delayed (and it has usually been resorted to only as a late or ultimate measure), the efficiency of the procedure diminishes proportionately, due to the development of secondary arthritic and periarthritic changes, yet even in these late cases one may anticipate relief of pain and functional improvement.

The attitude of some insurance companies and compensation groups, that excision of the carpal scaphoid is a very disabling procedure in itself, is unwarranted. The tendency to terminate these ununited cases with "lump-sum settlements" is especially injurious to the patient himself, who, left on his own, often fails to seek proper medical care and becomes a liability to his community.

We recommend total and not partial excision. The latter procedure, advocated by some authors in the belief that undue deformity might thereby be prevented, often results in continued disability. The scaphoid bone is removed

TABLE I

AN ANALYSIS OF EIGHT CASES OF EXCISION OF THE CARPAL SCAPHOID FOR UNUNITED FRACTURE

Case No	Name	Age	Sex	Wrist	Injury	Duration Since	Symptoms and Physical Findings	Roentgenologic Findings	Operation	Result
1	C G	23	M	Left	20 mos		Pain and localized tenderness in region of scaphoid. Restriction of motion especially of radial and dorsiflexion	Ununited transverse fracture of scaphoid with dislocation of proximal fragment. Slight lip-ping of radial styloid process	Total excision, 1932	Excellent. No pain or tenderness. Return of normal range of motion without apparent deformity. (This patient had been awarded total disability prior to operation)
2	E M	23	M	Left	3 yrs		Pain, tenderness and localized swelling in 'anatomic snuff-box'. Restriction of all movements of affected wrist especially of dorsiflexion and radial deviation	Ununited transverse fracture of scaphoid. Sclerosis and cystic degeneration of both fragments	Total excision 1931	Excellent. No pain or tenderness. Return of normal function and of normal range of motion. No apparent deformity. Successful professional boxer for past three years
3	D S	49	M	Left	6 mos		Same	Ununited transverse fracture of scaphoid with sclerosis of margins of pseudarthrosis	Total excision, 1932	Excellent. Many postoperative complaints disappeared following satisfactory financial settlement. Return of normal range of painless motion without apparent deformity
4	E C	29	M	Right	4 mos		Same	Same	Total excision, 1929	Excellent. No pain or tenderness. Restoration of normal function and motion, except for very slight restriction of dorsiflexion. No apparent deformity
5	H G	25	M	Right	6 mos		Same	Same	Total excision, 1925	Same
6	P P	21	M	Left	2 yrs		Same	Transverse fracture of scaphoid with nonunion. Distal fragment sclerotic and proximal fragment viable. Early osteo-arthritis changes	Unsuccessful drilling and bone graft 5 mos prior to total excision, in August, 1937	Good. No pain, tenderness or deformity. At present some restriction of dorsiflexion and radial deviation (one-half normal range), but with restoration of normal function. Result is steadily improving
7	F R	46	M	Right	2 yrs		Same	Ununited transverse fracture with moderate osteo-arthritis changes and cystic degeneration of both fragments	Total excision, 1922	Good. No pain or tenderness and range of motion normal in all directions except dorsiflexion and radial flexion (one-half normal). Function very good. There is no evidence of deformity
8	I D	44	M	Left	7 yrs		Moderate tenderness in region of scaphoid. Painful disability with restricted motion and impaired function of the affected wrist. Atrophy of disuse of forearm and hand musculature	Ununited transverse fracture with advanced osteo-arthritis changes of the radial articular surface and adjacent carpal bones	Partial excision (distal fragment) 1937	Poor. Continued painful disability and impaired function. No follow-up since 1932. Arthrodesis probably indicated

through a small incision, two inches in length, on the dorsum of the wrist, made directly lateral and parallel to the tendon of the extensor pollicis longus, and carried deeply to the bone, with the longus tendon retracted medialward. The capsule is split, and the carpal fragments removed completely by sharp dissection, care being taken not to traumatize the adjacent cartilaginous surfaces. A circular plaster bandage or volar splint is applied with the hand in ulnar deviation and slight dorsiflexion for seven to ten days until acute manifestations have subsided and thereafter, motion is encouraged.

Analysis of Cases—To substantiate these contentions, a follow-up study of eight cases of excision, seven total and one partial, is herewith presented. Two additional cases of total excision are excluded because of insufficient data. Three of the cases are presented by courtesy of Dr. George P. Muller, from his service records at Jefferson Hospital, and one from the private records of Dr. Lynn Rankin. The cases in this series have either been recently examined or contacted through a questionnaire.

Our experience with the drilling-bone graft procedure has been limited to two cases. One, an instance of nonunion of two years' duration failed to unite without improvement, while the other, of eight months' duration, secured bony union but continued to complain of some pain and disability.

The eight cases of ununited carpal scaphoid were all males, their ages varying from 21 to 49. All had sustained severe injuries to the wrist, five on the left side and three on the right, and none had had the benefits of an efficient conservative regimen. The duration from the time of injury varied from four months in one, to six months in two, 20 months in one, two years in two, three years and seven years in one each.

All complained of pain, limitation of wrist motion, and disability, and all evidenced some restriction of motion, especially dorsiflexion and radial deviation, swelling, tenderness in the anatomic snuff-box, and atrophy of the forearm muscles.

The roentgenograms showed definite pseudarthrosis in each case, with varying degrees of sclerosis, vacuolization and fragmentation, the degree of degenerative and proliferative changes increasing with the duration of the nonunion.

Total excision was performed in all but the oldest case of seven years' duration, six months ago in one, and from five to 15 years ago in the remainder.

The results in five cases are considered very good or excellent with regard to anatomic, functional and economic restoration. These patients have no pain or tenderness and have returned to their former or similar occupations with normally functioning wrists. One patient has continued his professional boxing. They show little or no limitation in wrist motion, nor is there any clinical evidence of anatomic deformity, although postoperative roentgenologic studies in two cases show slight radial deviation of the wrist, as the multangular bones tend to partially occupy the space left by the extirpated scaphoid.

It is of interest that one of these successful results, a nonunion of 20 months'

duration, had been compensated for "total disability" prior to operation as a *Clinic* patient, and that another, who had complained of continued disability following excision, had experienced a complete recovery immediately following a substantial settlement

The results in two cases, each with nonunion of two years' duration, are considered as good. These patients have no pain or tenderness and, despite moderate restriction of motion, have useful wrists. Both cases showed considerable disability prior to operation with roentgenographic evidence of complicating osteo-arthritis, and both are satisfied with their results.

One case, an instance of nonunion of seven years' duration, with painful disability and with roentgenologic evidence of advanced osteo-arthritis complicating the pseudarthrosis, had had a partial excision with only moderate relief of pain and with persisting impairment of function. This result is classed as a poor one.

CONCLUSIONS

The operation of total excision must be considered in the rational therapy of ununited fracture of the carpal scaphoid (navicular) bone. When utilized early, before secondary arthritic and periarthritic changes take place, a very satisfactory result with regard to anatomic, functional and economic recovery may be anticipated.

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THE OSSEOUS SYSTEM IN HODGKIN'S DISEASE

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INVOLVEMENT of bone in Hodgkin's disease is no longer to be regarded as being so rare that it should be considered of comparatively little importance. There is still a great tendency to refer all symptoms to lymphatic involvement and only as a last resort to investigate the osseous system.

The writer has been unable to find any comprehensive statistics regarding incidence. This is due to the relatively infrequent osseous studies which have been made, and also to the terminology currently used. Particularly confusing is the inclusion of the leukemias, lymphosarcoma and Hodgkin's disease under the classification of lymphoblastoma, since the roentgenologic appearance of all may be very similar. Review of the literature reveals wide variation. About 10 per cent incidence is reported by some, while others believe it to occur, at some time in the course of the disease, in 100 per cent. Symmers¹⁷ found osseous changes in seven of his 15 cases, or 46.6 per cent, while Craver and Copeland⁵ reported 15.7 per cent involvement in 172 patients with Hodgkin's disease. Ten consecutive, unselected patients, referred to the Radiation Therapy Department of the Brooklyn Cancer Institute, with a diagnosis of Hodgkin's disease, constitute the cases to be reported. It will be noted in Tables I and II that eight proved to have Hodgkin's disease, and that the final diagnosis in one was lympho-epithelioma and in the other lymphosarcoma. Of these eight patients, four had typical bone lesions, two showed changes characteristic of Hodgkin's disease, and the other two showed no bone changes. The incidence in this group is, therefore, 50 to 75 per cent, 25 per cent being reserved for possible final verification. It is believed that bone involvement would be found much more common if routine and repeated roentgenologic examinations of the osseous system were made.

Whether invasion of the osseous system is primary or secondary is still a matter of discussion (Hultén,¹¹ Lockwood, Johnson and Narr,¹³ Ginzburg,⁸ Spencer and Dresser,¹⁶ Aschoff¹). It is the opinion of some that primary bone involvement never occurs. However, in a disease of such variable manifestations and histologic characteristics, it is believed that the probability of such occurrence should be borne in mind, at least until proved otherwise. Blount³ reported a case in which bone changes preceded demonstrable lymph node involvement by two years, and Montgomery¹⁴ cites an instance in which lymph node involvement was not demonstrated until two and one-half years after the onset of the disease. Herschel¹⁰ reported bone marrow and liver involvement without apparent invasion of lymph nodes, and Krumbhaar¹²

described a case of bone marrow and spleen involvement and no lymph node pathology after careful search at autopsy Bone invasion may, of course, also occur by erosion from neighboring diseased lymph nodes, as shown in Table II, Cases 1 and 4

TABLE I

Case No	Age* Sex	Duration of Present Illness	Biopsy or Necropsy		Final Diagnosis
			Hodgkin's Disease	Eosinophilia	
1	20 M	9 yrs	+	Marked	Hodgkin's disease
2	29 F	4 yrs 4 mos	+	Moderate	Hodgkin's disease
3	29 F	7 yrs	+	Marked	Hodgkin's disease
4	33 F	3 yrs 2 mos	+	Marked	Hodgkin's disease
5	16 F	1 yr 5 mos	+	Marked	Hodgkin's disease
6	32 M	1 yr 2 mos	+	Marked	Hodgkin's disease
7	13 M	2 yrs	+	Marked	Hodgkin's disease
8	21 F	1 yr 1 mo	+	Moderate	Hodgkin's disease
9	37 F	2 yrs 5 mos	0	Moderate	Lympho-epithelioma
10	40 M	9 mos	0	Slight	Lymphosarcoma (lymphoblastoma type)

* At onset of present illness

TABLE II
OSSEOUS INVOLVEMENT

Case No	Symptoms and Time of Appearance*	Roentgenographic Findings				Location	Result of Therapy	
		First Observed*	Osteoplastic	Osteolytic	Erosion		Clinical	Roentgenographic
1	Pain left cervical region, 8 yrs 6 mos	6 yrs 8 mos	+		+	2nd, 3rd, 4th and 5th cervical vertebrae	Poor	None
2	Pain, dorsolumbar region, 3 yrs 5 mos	3 yrs 7 mos	+	+		11th dorsal, 2nd lumbar	Excellent	Hyperplasia
3	Dorsolumbar pain, 6 yrs 4 mos	6 yrs 7 mos	+	+		10th dorsal, 3rd lumbar	Very good	Lytic and hyperplastic
4	Pain rt arm, 14 mos	13 mos		+	+	Rt 1st 2nd rib and rt clavicle	Poor	Progressive
5	Pain lower end rt femur, 15 mos	3 mos	+	+		Lower end rt femur	Very good	Not treated hyperplasia
6	Pain lumbosacral and pelvis, 8 mos	7 mos	+		+	Lt 1st and 2nd rib	No change	Not treated no change
7	Pain lumbar left shoulder, 2 yrs	—	0	0	0	—	—	—
8	0	—	0	0	0	—	—	—
9	0	—	0	0	0	—	—	—
10	0	—	0	0	0	—	—	—

* After onset of present illness

Roentgenographic evidence of Hodgkin's disease of bone is usually demonstrated late. The involvement, however, may occur early as may be noted in Table II. The development and progression of the process is variable. Only by considering osseous studies as routine, as those made of the chest, can accurate statistics regarding probable time and mode of involvement be determined.

The lesions are usually multiple and may apparently occur in any part of the osseous system. The distribution in order of frequency, as reported by Spencer and Dierser,¹⁶ is spine, pelvis, sternum, ribs, skull and extremities. The spine, ribs, clavicle and possibly the femur and tibia were involved in the present series.

The frequently early, predominant reticulo-endothelial cell hyperplasia or the late lesion demonstrating fibrosis, and very little if anything more, are likely to be very confusing. The characteristic picture is one of hyperplasia of the lymphoid and endothelial cells together with Hodgkin's giant cells and eosinophiles. Later these cells are replaced by fibrous tissue, and at times caseation necrosis with a varying degree of hyperplasia of the marrow (Aschoff,¹ Barron,² Ewing⁶). However, the sections may and have been confused with Ewing's tumor, forms of myeloma, hypernephroma, malignant tumors and chronic osteitis. The variation of the histologic picture in various stages of the disease accounts for much of this confusion. Montgomery¹⁴ suggests that a marked eosinophilia in the tissue sections points to irritation and involvement of bone. Table I shows instances of marked eosinophilia in six of the cases of Hodgkin's disease and of moderate occurrence in two. One case with bone involvement showed moderate and the remainder marked eosinophilia. According to these findings osseous involvement was demonstrable roentgenographically in the presence of a moderate to marked eosinophilia. It is, however, believed that at the present stage of our knowledge lack of a marked eosinophilia should not be interpreted as absence of bone involvement.

The roentgenographic appearance of the lesions may be osteoplastic, osteolytic or a combination of the two. Figures 1(B) and 2(A) demonstrate these processes. According to Geschickter and Copeland,⁷ there may also be a marked periosteal proliferation. Unfortunately most of the cases described in the literature consist of the late or terminal stages. Figure 4(A), Case 5, shows a small mixed lesion in the lower end of the right femur. This may be a simple cyst, but since Hodgkin's disease of bone may resemble cysts, and since it demonstrates plastic and lytic changes, it must at least be considered as a possible early lesion. It is also of interest to note in Figure 4(B), taken a little more than one year after Figure 4(A), that the process has decreased in size and that the sclerosis at the margins has increased. This may be a retrogressing lesion. Further study will be necessary to definitely determine this. It appears somewhat similar to the process in the tibia in Figure 3(A), Case 2. This patient also has typical involvement of the spine as shown in Figure 2(A). Figure 5(A), Case 6, shows an area of erosion

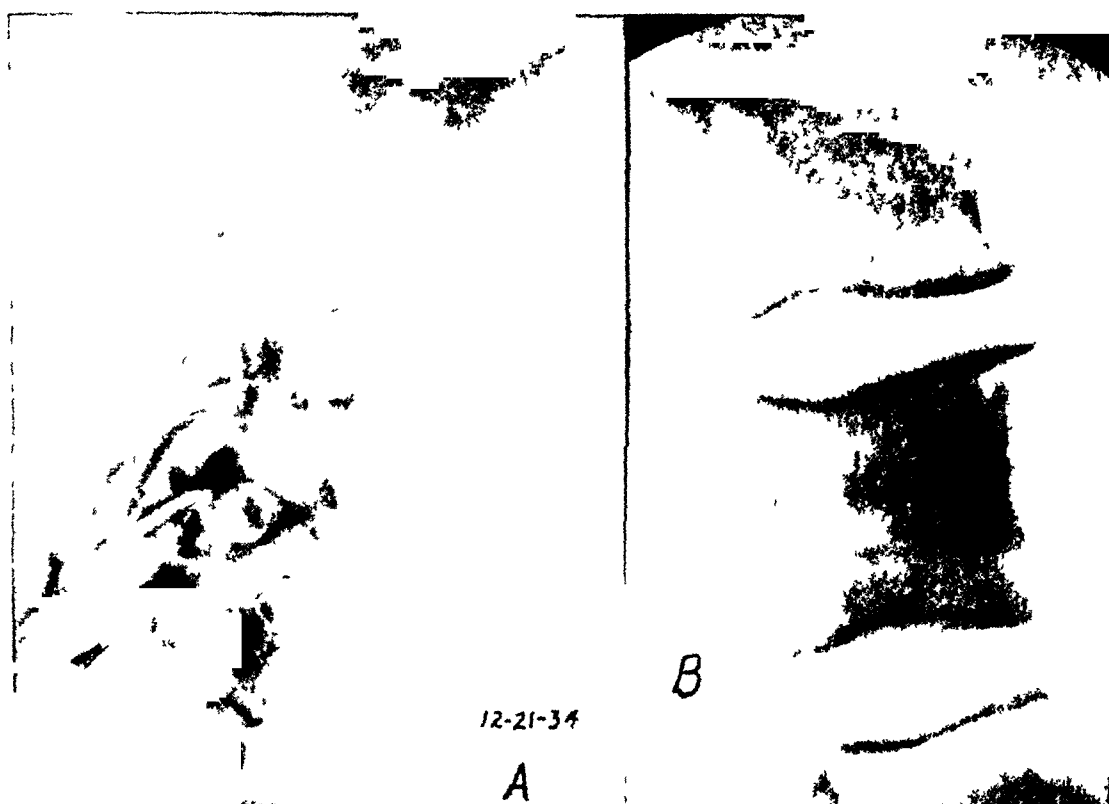


FIG 1—Case 1 (A) Showing erosion of the second third fourth and fifth cervical vertebrae and the large retropharyngeal mass (December, 1934) (B) Case 3 Demonstrates the osteolytic and osteoplastic process involving the third lumbar vertebra



FIG 2—Case 2 (A) Shows the predominating hyperplastic process in the eleventh dorsal vertebra (B) Case 1 Demonstrates the radon seeds and marked reduction in the size of the retropharyngeal mass. No demonstrable change is noted in the extent of erosion of the cervical vertebrae, but sclerosis is now present (February, 1937)

in the first rib and bone condensation in the second. The latter may be an associated melorheostosis, but must be followed to definitely determine its significance. The latest roentgenologic findings in Case 4 (Fig 5[B]) no doubt represent Hodgkin's involvement combined with superimposed pyogenic infection. However, erosion of the clavicle and second rib in this case was noted initially, 13 months after the onset of the present illness, and, therefore, before any evidence of abscess, as will be shown later. Figures 1(A) and 2(B), Case 1, demonstrate the deep excavation in the cervical vertebrae due to erosion by neighboring diseased tissue. The marked destruction of the posterior surfaces of some of these bodies is well demonstrated only in the radiographed section (Fig 3[B]). There was no roentgenologic evidence of paraspinal soft tissue distortion in these cases.

Hodgkin's disease of bone may be confused with the changes due to carcinoma, multiple myeloma, chronic osteomyelitis, Ewing's tumor, hypernephroma, tuberculosis, leukemia, lymphosarcoma and cysts. Fortunately, in the more common, typical cases no confusion arises. At times the diagnosis can be made only after biopsy, which, as previously indicated, may itself be very confusing. A marked response to roentgenotherapy, such as occurred in Cases 2 and 3, Table II, may give a clue to the diagnosis. However, lymphosarcoma and leukemia may respond in the same manner. In those cases of bone lesions presenting an atypical roentgenographic picture and unusual clinical manifestations, the possibility of Hodgkin's disease should always be considered. In no roentgenologic study are a detailed history, repeated blood studies and biopsy, where possible, more essential.

Pain may be the first indication of possible bone involvement. However, pain referable to the region of certain bones and joints may be present and no disease found in these bones as illustrated in Cases 6 and 7, Table II. Conversely, bone lesions are undoubtedly often present before symptoms appear. In Cases 2 and 3, Table II, initial roentgenographic evidence of bone disease was demonstrated just two months and three months, respectively, after onset of symptoms. In Case 1 the symptoms directly referable to bone and nerve destruction occurred 22 months after the bone lesions were initially demonstrated. Also in Case 4, the bone lesions were observed before the onset of symptoms. The symptomatology is essentially dependent upon the anatomic location of the lesion and the degree of functional impairment. Consequently, the symptoms may vary from none to excruciating pain, marked impairment of function, pathologic fractures, deformities and a variety of neurologic conditions, such as anesthesia, hemiplegia, paraplegia, transverse myelitis, etc.

Roentgenotherapy offers palliation, remission and retards progress of the disease in many cases. Osteolytic areas may be replaced by bone, but an osteoplastic appearance, contrary to reports in the literature, is not necessarily an indication of previous radiation therapy. This is demonstrated in Cases 2 and 3, in which dense areas in the vertebral bodies were seen on first examination and prior to treatment of the spine.

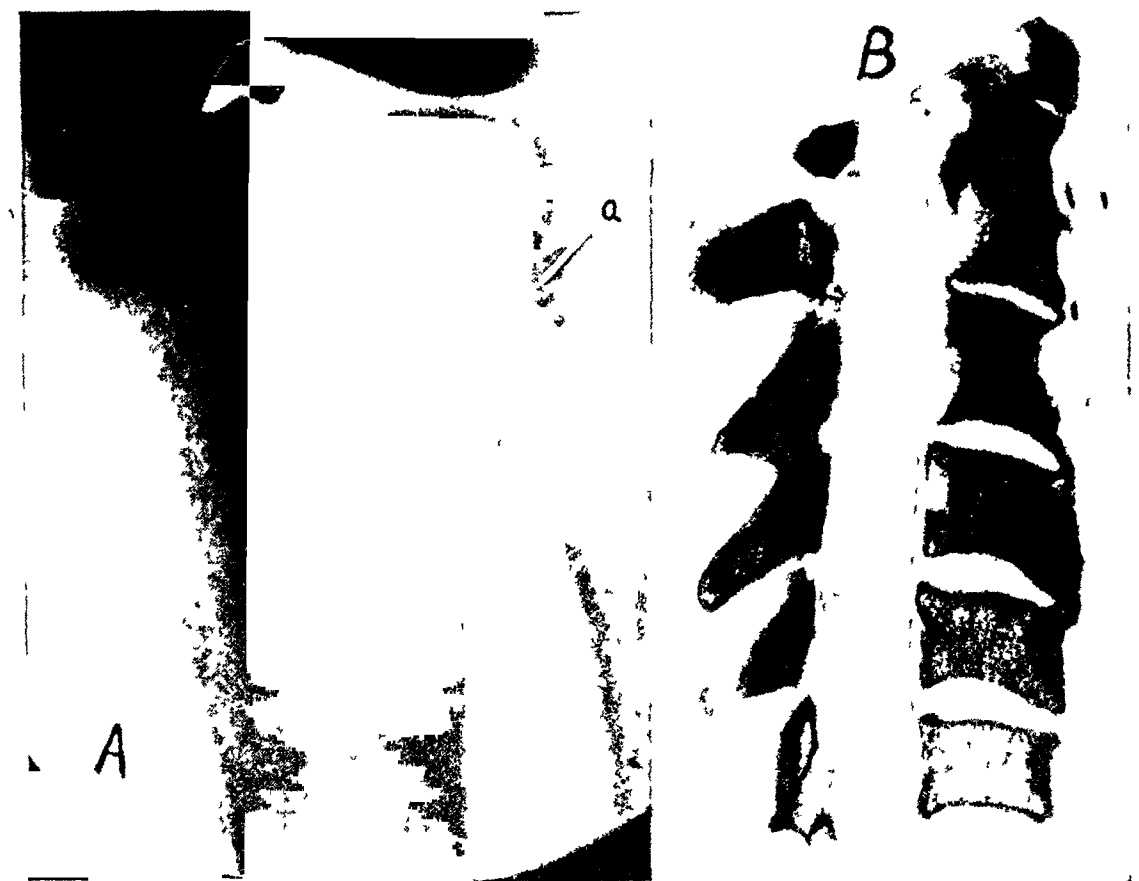


FIG 3—Case 2 (A) Showing the small osteolytic process (a) in the tibia (B) Case 1 Roentgenogram of section demonstrating particularly the extent of erosion of the posterior aspects of the vertebrae, which could not even be demonstrated well in a roentgenogram of the unsectioned specimen

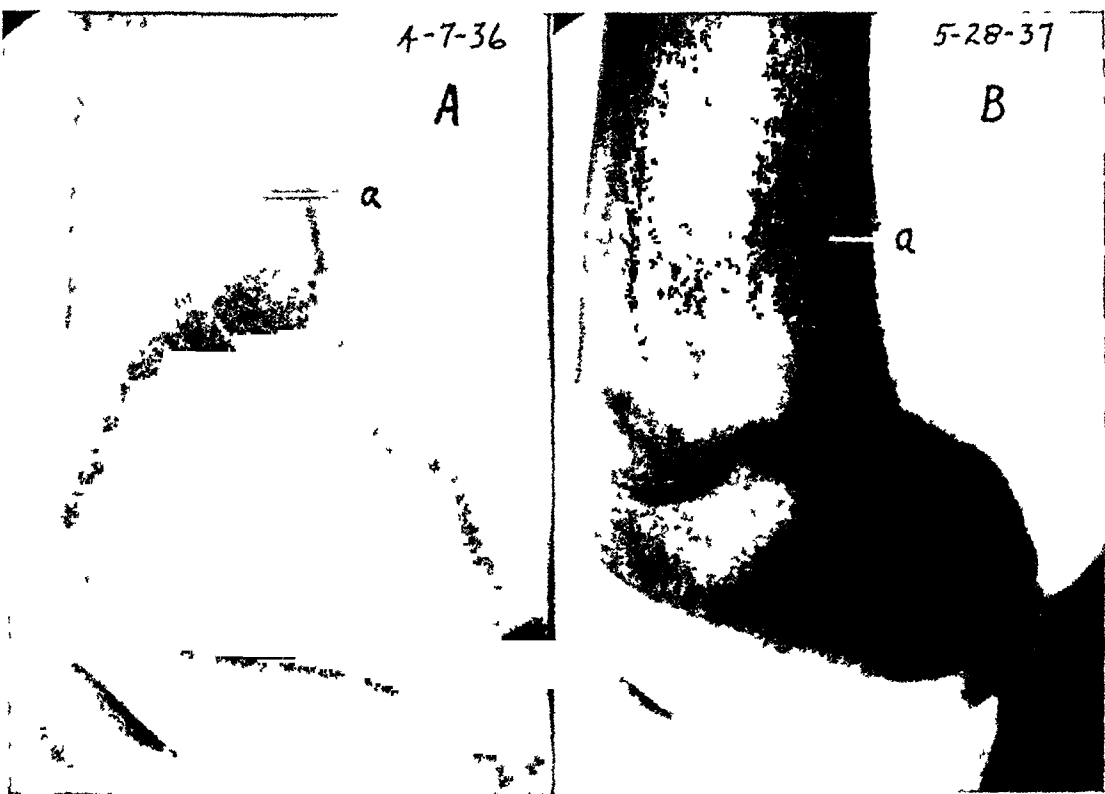


FIG 4—Case 5 (A) Showing osteolytic process (a) in the femur (April, 1936) (B) Demonstrates decrease in size of the lesion and sclerosis of the margins (a) (May, 1937)

Whether there is any effect of roentgenotherapy to distant areas of lymph node involvement on the bone lesions is not definitely known. Case 2, however, demonstrated that in spite of extensive therapy through four pelvic ports for diseased inguinal nodes and irradiation along the entire left pelvic wall, the patient continued to have excruciating pain, which was only relieved shortly after therapy to the spine had been instituted. It was observed in other cases that radiation was only effective when directed to the affected part. The technic usually employed in these cases was 200 K V, 20 Ma, 50 cm FSD, 0.5 Mm Cu and 1 Mm Al filtration, 200 r (measured in air) to each port every other day. Two paravertebral fields (5x15 cm) were ordinarily used in the spine cases. In those cases favorably influenced by radiation, marked improvement was noted after about 1,000 r to each port. Case 2 obtained marked relief after 400 r to each port. The average total dose was 2,000 r to each port. It is believed that radiation should be administered to relieve symptoms and prevent deformities. The bone lesions, with or without the presence of symptoms, should be periodically checked so that, where possible, complications may be avoided before the process becomes too far advanced. Osseous involvement, if diagnosed early and treated, may not only add to the active life span of the individual but will often spare him the agonies which may accompany the complications.

Space does not permit a detailed history of each case, but since Cases 1 and 4 present particularly interesting features they will be presented briefly.

Case 1—The present illness began in 1928, at which time there were palpable cervical, axillary and inguinal nodes. The patient did well under high voltage therapy and permanent interstitial radiation (sixteen 1 mc, 0.3 Mm gold seeds, total 2,128 mc hrs). In October, 1936, he complained of continuous pain in left side of neck. In March, 1937, numbness and tingling developed in hands and weakness in both upper extremities together with involuntary twitchings in the upper and lower extremities and a cord bladder. Examination revealed evidence of pyramidal tract involvement. There was no response to roentgenotherapy and the patient expired in April, 1937. At necropsy, dense necrotic tissue containing lymphocytes and plasma cells was present between the anterior surface of the vertebral bodies and the posterior wall of the pharynx. In some areas the marrow was replaced by dense, poorly cellular fibrous tissue, while in others it contained myeloid and plasma cells and in the fifth and sixth cervical vertebrae there were, in addition, large numbers of erythrocytes. The spinal canal showed shallow erosion of the bony posterior surface at the level of the second, third and fourth vertebral bodies. The meninges in the region of the upper three involved vertebrae were replaced by dense fibrous tissue which included peripheral nerve bundles in various stages of atrophy. Lymph nodes were notably scarce. A firm markedly fibrotic supraclavicular node was present, and also a somewhat larger mass in the right upper anterior mediastinum, which showed much fibrous tissue, few lymphocytes and plasma cells, hemorrhage and calcific deposits. The lungs showed purulent bronchopneumonia.

Case 4—Present illness began, in August, 1933, with bilateral swellings of the neck. Fourteen months later, the patient complained of pain in the right arm. The lesions in the second rib on the right side and in the right clavicle were demonstrated one month prior to this complaint. A right Horner's syndrome developed. In June,

1936, a bleeding sinus appeared in the right supraclavicular area and the swelling in this region broke down. The base of the wound became covered with a necrotic exudate. This patient never responded well to roentgenotherapy.

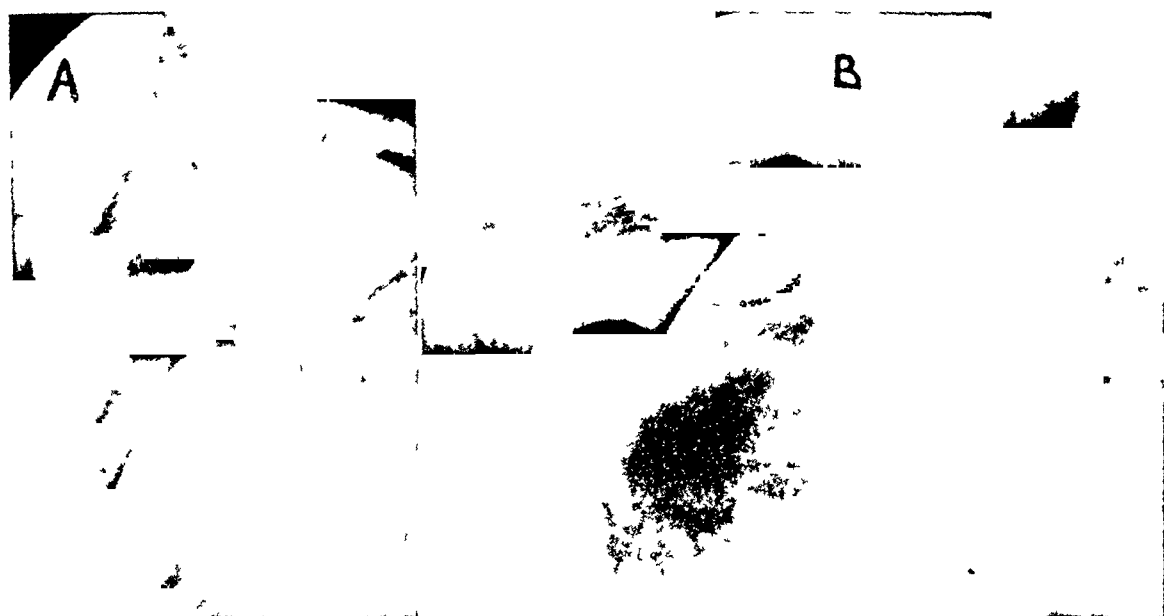


FIG 5—Case 6 (A) Demonstrates indentations in the first rib and the area of bone condensation in the second. (B) Case 4. Showing erosion of the outer third of clavicle and similar aspect of the first and second ribs together with thickening of the pleura. The lesion in the clavicle and second rib was present in 1934 and progressed slowly. There was no abscess at this time.

SUMMARY

A thorough review of the literature, case reports and general observations have been presented relative to involvement of the osseous system in Hodgkin's disease. The following were considered: Incidence, mode, time and type of bone involvement, distribution, histology, symptoms and time of their appearance, diagnosis and treatment.

Early diagnosis and treatment of Hodgkin's disease of the osseous system cannot be overemphasized.

In cases of bone lesions presenting an atypical roentgenographic appearance and unusual clinical manifestations, the possibility of Hodgkin's disease should always be considered.

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SUBLINGUAL EPIDERMOID CYSTS

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THE following four cases of true epidermoid cysts arising in the floor of the mouth have been observed in 54,000 surgical specimens examined in the Pathologic Laboratory of St Luke's Hospital, New York, during the past 40 years. Each of the four cysts was lined with stratified squamous epithelium and two contained hairs or hair follicles.

Case 1—I S, female, age 16, was admitted to St Luke's Hospital December 9, 1900, Service of Dr Robert Abbe. A small lump was noticed on the floor of the mouth beneath the tongue when the patient was age eight. At first it increased only slightly in size, but during the past few years its growth had been more rapid. At one time the tumor had opened and discharged a small quantity of thick, yellowish fluid tinged with blood.

Examination showed a soft, fluctuating tumor mass which could be seen and felt beneath the chin and which projected into the floor of the mouth beneath the tongue. It occupied a midline position. At operation the tumor was aspirated and removed through a transverse incision in the floor of the mouth. The mass was soft, cystic, bean-shaped, and measured 5 by 4 by 2.5 cm. The contents of the sac were yellow, greasy and contained a few hairs. Histologic study showed the cyst to be lined with stratified, squamous epithelium, with underlying sebaceous glands and hair follicles.

The patient was discharged, apparently cured, on the fourth postoperative day. No follow-up record is available.

Case 2—D S, male, age 2½ years, was admitted to St Luke's Hospital December 18, 1929, Service of Dr Frank S Mathews. A mass in the floor of the mouth was first noticed shortly after birth. It had gradually increased in size but had not produced any symptoms. There were no other congenital abnormalities.

Examination showed a cystic mass about 1 cm in diameter situated in the floor of the mouth just lateral to the midline. It was nontender, did not fluctuate and was not fixed. A clinical diagnosis of a dermoid cyst of the floor of the mouth was made. At operation the cyst was opened, emptied of its contents and the wall excised. The specimen measured 1 by 0.75 by 0.2 cm. Histologic study showed a very thin-walled cyst with a lining which was intact in some areas and composed of squamous epithelium. Other areas of the lining were considerably altered by inflammatory changes and underlying fibrosis. There was lymphoid infiltration throughout but no evidence of malignancy.

The patient was discharged on the second postoperative day. No follow-up record is available.

Case 3—L P, male, age 2½ years, was admitted to St Luke's Hospital June 9, 1933, Service of Dr Henry H M Lyle. A painless tumor was first noticed under the tongue and beneath the chin when the patient was about 18 months old. The mass had steadily increased in size but had not reached proportions where it interfered with talking or eating.

Examination showed a small reddish protuberance at the opening of the left sublingual duct. Beneath the mandible in the neck, to the left of the midline, there was a soft, smooth, freely movable, nontender, fluctuant mass about 5 cm in diameter. At operation a transverse incision was made through the mucous membrane of the floor of the mouth,

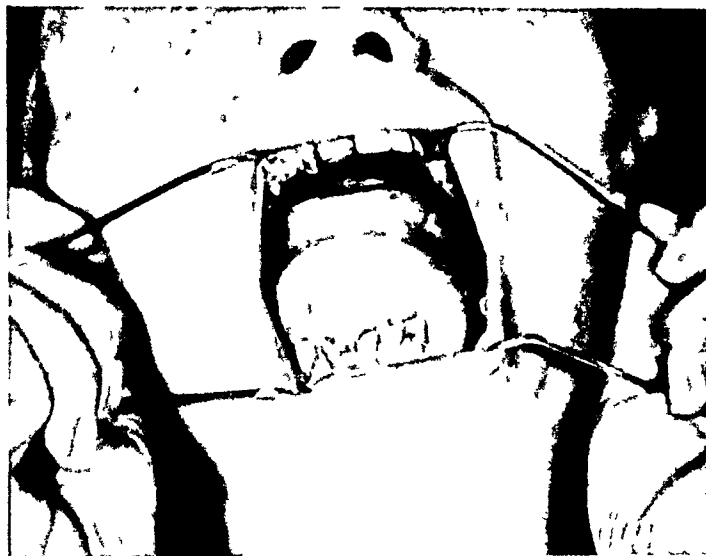


FIG 1—Case 4 Photograph of patient showing cyst in floor of mouth beneath tongue



FIG 2—Case 4 Photograph of excised specimen



FIG 3—Case 4. Photomicrograph of cyst wall showing the inner lining of stratified squamous epithelium supported on a definite connective tissue base

pressure was applied to the cyst beneath the chin, and the mass was removed. The specimen was cystic and measured 4 by 3 by 3 cm. It was filled with yellowish-white creamy material. Histologic study showed the lining to be composed of squamous epithelium which was somewhat inflamed. There was a slight papillary down-growth into the corium and loose connective tissue. Hair follicles and hypertrophic sweat glands and one rather large duct lined with squamous epithelium containing desquamated cells, were also seen. The epithelial cells showed varying stages of atrophy and hyperplasia with some hyperkeratinization.

The patient was discharged, apparently cured, on the fourth postoperative day. No follow-up record is available.

Case 4.—E. A., female, age 37, was admitted to St. Luke's Hospital October 14, 1936. The patient had first noticed a mass beneath her chin about 20 years previously. It had gradually increased in size and had risen in the floor of the mouth, displacing the tongue upward. It was aspirated twice eight years and six weeks ago respectively before admission to the hospital, with only temporary relief.

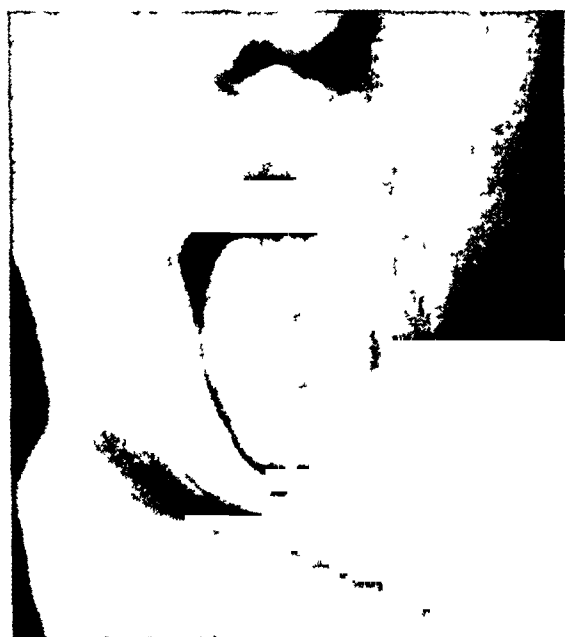


FIG. 4.—Case 4. Photograph of patient after operation showing normal extension of tongue.



FIG. 5.—Case 4. Photograph of patient after operation showing tongue in normal position.

Examination showed a large, soft, non-tender cystic mass lying in the midline of the floor of the mouth and displacing the tongue upward (Fig. 1). It could also be seen and felt as a soft midline tumor beneath the chin in the submental region. A diagnosis of sublingual dermoid cyst was made. Under colonic ether anesthesia, a transverse incision was made over the cyst in the floor of the mouth. The mass was dissected from the surrounding structures and removed intact. The resulting dead space was partially obliterated by sutures and the remaining cavity was packed with iodoform gauze. The excised cyst measured 8 by 5 by 3 cm (Fig. 2). The surface was smooth and the wall was thin. The cyst contained thick, white cheesy material but no hairs. Histologic study showed the lining to be composed of squamous epithelial cells supported on a layer of fibrous tissue. The epithelium had all the characteristics of cutaneous epithelium with a keratinized layer on the surface (Fig. 3). There were no hair follicles or sweat glands.

The patient was discharged on the third postoperative day. She has been seen at regular intervals since, is completely symptom-free, and has normal function of the tongue (Figs. 4 and 5).

Discussion.—Sublingual dermoid or epidermoid cysts are derived from fetal remnants in the mesobranchial field¹ and should be clearly differentiated from the more common ranulae. The latter are the result of cystic degenera-

tion in the sublingual gland, are usually unilateral and are lined by flattened cuboidal epithelium. They are thin-walled, contain a fluid resembling saliva, and are difficult to remove surgically without rupture. Sublingual epidermoid cysts, on the other hand, arise in a midline position, are lined with stratified squamous epithelium, and possess a definite connective tissue supporting framework, giving them a thicker and tougher wall and making surgical removal without rupture easy. Although these cysts arise in a midline position, increase in size may cause them to be displaced to one side so that they appear to have a unilateral origin. Other epithelial, cutaneous structures, such as hair follicles and sebaceous glands, may be present, as in two of the cysts herewith reported, but other congenitally misplaced remnants, such as nervous or osseous tissue have not been observed.

Treatment—Surgical excision is the treatment of choice for these cysts. Adequate exposure through a transverse incision in the mucous membrane overlying the cyst, gentleness and sharp dissection with a knife or scissors, makes excision of the entire cyst wall and contents relatively simple. Although the cavity beneath the tongue which follows the removal of a cyst may be surprisingly large (Case 4) it can be completely obliterated by sutures and packing. Normal position and function of the tongue are to be expected following the operation. Aspiration, whether for diagnosis or relief of symptoms, has little to commend it, is rarely actually indicated, and may possibly lead to serious infection of the cyst wall and floor of the mouth.

Injection of various irritating, sclerosing solutions into all sorts and kinds of hollow structures, with little regard to the character of their lining or supporting wall, has been widely employed and recommended in the past few years, and was even seriously suggested as an elective form of treatment in Case 4. The principle underlying the obliteration of cavities lined with tissues of mesodermal origin by the production of irritation, fibroblastic proliferation and fibrosis, is relatively simple and easily understood. In the case of structures lined with various kinds and thicknesses of epithelium, however, the complete destruction to the last cell by a sclerosing solution must be accomplished before this fibroblastic activity and fibrosis can take place. This is quite a drastic form of therapy, highly uncertain as to its outcome, and can in no way be considered a satisfactory substitute for clean surgical excision. It is certainly to be condemned as a method of treatment of sublingual epidermoid cysts.

SUMMARY

Four cases of true epidermoid cysts arising in the floor of the mouth are reported. These cysts arise from fetal remnants in the mesobianchial field, are lined by stratified squamous epithelium, and should be clearly differentiated from the more common ranulae. Surgical excision while the cysts are still small and uninfected is the elective form of treatment.

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THE REGENERATION OF SENSATION IN TRANSPLANTED SKIN

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THE regeneration of sensation in transplanted skin and the degree to which this regeneration takes place represents an important factor from both a clinical and an academic standpoint. Clinically, its importance lies in the selection of the type of graft for use in covering defects where the sense of touch is needed for proper function. The type of graft to be used in such a case is obviously the one in which the earliest return of good sensation can be assured. From an academic standpoint, it gives us an excellent means of studying the mechanism of nerve regeneration and the relationship of the various forms of sensation developed in the sensory nerve endings. Until recently, however, the literature contained few references to the subject and no detailed study of nerve regeneration in skin grafts alone had been attempted.

Kredel and Evans,¹ in 1933, J S Davis and Kitlowski,² in 1934, and Loyal Davis,³ in 1934, reported their findings in a series of cases which represented a combined total of 188 grafts. Of these, 102 were pedicle flaps, 38 were free full thickness grafts, 24 were Thiersch grafts, nine were split thickness grafts, and 15 were pinch grafts. All agreed that sensation returned first, and was more complete, in pedicle flaps than in any other type. Next in order was the free full thickness, then the split thickness, and finally the Thiersch graft. From this, it was concluded that the rate and degree of return, other things being equal, were directly proportional to the thickness of the graft used. All agreed that there was a temporal dissociation in the recovery of pain, touch and temperature sensations. They also agreed that return of sensation began about the periphery of the graft, with the first evidence of recovery present in the proximal portion progressing distally and from the sides. Loyal Davis states, however, that return of sensation in Thiersch and free full thickness grafts may occur in patches. He also states that recovery is more rapid in those pedicle grafts which have only a small amount of subcutaneous tissue attached to the skin. These two points represent the only element of question in the general conclusions of all three authors.

Since pedicle flaps represented the majority of grafts in their cases, and since only a few split thickness grafts were included, a detailed study of the return of sensation in this latter type was attempted. In order to have a comparative study, several free full thickness grafts and a few pedicle grafts were also included. The patients used varied in age between five and 15 years. No patient was selected for study if there was any question about the ability to

cooperate well. All three of the above named authors included cases within this age group, and all concluded that age was not a factor in the recovery of sensation. Most grafts were performed for the release of scar contractures or the covering of defects, the result of burns.

Method of Study—Tests for sensation were begun at the time of the first or second dressing, the fifth or sixth day after the application of the graft. They were made daily in each case for several days, and later one each week. Most grafts were followed until sensation was not only present, but also equal to that of normal skin proximal to the graft and in other parts of the body. Complete return of sensation cannot be considered as present until this stage has been reached. For testing response to pin prick, an algesiometer, delivering a pressure of 0.7 Gm. by gravity, was used so that the amount of force applied would be constant in all cases. The instrument used consisted of the "inner works" of a "Redipoint" mechanical pencil, with an ordinary sewing needle anchored in the lead container. The response to this is listed as the return of pain in the grafts of this series. For testing the return of touch, a small wisp of cotton drawn to a fine point was used. Completeness of the return was also checked by a comparison of the two-point discrimination of the graft with that of normal skin. Temperature discrimination was tested in many instances, but the findings in this were not such that conclusions could be drawn. With the ordinary means of testing temperature response, one cannot be certain that the response is primary in the graft itself. There is always the possibility that the sensation may be the result of transmission of the heat or cold to the underlying structures. The recovery of temperature sense will, therefore, not be included in this report. The growth of hair in children is not sufficient to necessitate shaving of the grafts prior to testing in most instances.

It may be argued that return of sensation in split thickness grafts cannot be estimated satisfactorily since they are so thin that impulses in the usual methods of testing will be transmitted through the grafts to the underlying structures. This is certainly not the case, however, when an algesiometer delivering such a light pressure is used for pain, and a wisp of cotton is used for touch. If this were true, the return should be complete at the time of the first examination instead of being anesthetic for the first few days, as is true in most instances. Neither can this be considered a factor when the graft is followed until its sensation is equal to that of normal skin in other parts of the body.

Split Thickness Grafts—Forty-five split thickness grafts were studied during a period of three years, the majority of which were followed long enough to definitely establish the time of complete sensory regeneration and be certain that this was not merely an early hyperesthesia. Contrary to previous reports, return of sensation occurred over all parts of each graft simultaneously, and, with three exceptions, there was no evidence of regeneration from the margins of the graft. One of these three exceptions (Graft No. 3), was a graft applied to cover the donor area of a recent pedicle flap in the thigh in which the full thickness of both skin and subcutaneous tissue had been

removed. Pain and touch returned over the entire graft at the same time, but progression from this point to equal the sensation of normal skin occurred from the proximal and lateral margins. In the second (Graft No. 10), the graft was placed on an excellent subcutaneous tissue bed except for a portion overlying a completely denuded flexor profunda tendon in the ring finger. Except for this portion, the graft equaled the sensation of normal skin at 22 days, and had returned over all parts of the graft at the same time. Over the exposed tendon, however, where a complete take in the graft was also obtained, the return was definitely from the proximal and lateral margins, progressing distally very slowly. Return in the distal portion of this area was not equal to



FIG. 1—Scar of moderate density involving dorsum of foot. There is no involvement of the deeper structures and a satisfactory subcutaneous tissue bed is available after excision of the scar.



FIG. 2—(Graft No. 7, Table I). Same as Fig. 1, after application of split thickness graft. Return of both pain and touch to equal normal skin was present at the end of 60 days and occurred over all parts of the graft simultaneously.

normal skin until 110 days. In the third (Graft No. 4), after both pain and touch had shown complete return in the usual manner, though not yet equal to normal skin, the central portion of the graft became elevated by a collection of sebaceous material secreted beneath it. Sensation over this area was immediately lost completely and subsequent return occurred very slowly from the proximal margin. This portion was not equal to the sensation of normal skin until after 55 days. In all other grafts, return of sensation appeared in scattered areas over the entire graft, then spread rapidly to completion in both pain and touch. The improvement to equal the sensation of normal skin took place more slowly. In all cases except four the increase in sensation, however, was one of steady progression from the first evidence of return until the complete stage was reached. In these four grafts (Nos. 7, 20, 30 and 33), there was definite evidence of early hyperesthesia which soon subsided, then progressed in the usual manner. In Graft No. 21, a portion of the transplant was

placed directly upon the exposed median nerve, and in Graft No 34, upon the exposed tibial nerve. The portions overlying these nerves were extremely hypersensitive from the very beginning, but this disappeared as subcutaneous tissues were reformed.

There was a temporal dissociation demonstrable in the return of pain and touch in all grafts except in those where both showed complete return at the time of the first dressing or first examination. This element was not as marked in this series, however, as in the previous reports.

Return of sensation in split thickness grafts has been found to be much more rapid than previously supposed, and they showed the earliest complete



FIG 3—In contrast to Fig. 1 this shows a dense extensive scar, the result of a very deep burn. The deeper structures are involved in this type of scar, and the graft must be placed on a scar tissue base or sometimes directly upon muscle instead of upon normal subcutaneous tissue. Obviously, the return of sensation would be markedly delayed.

return of any of the various types. This regeneration at the same time is just as complete as in any of the others. In 16 of these grafts, there was regeneration in both pain and touch equal to that of normal skin within 60 days or less. This more rapid return, which takes place over the entire graft simultaneously, seems to indicate that the regeneration is not dependent upon the longitudinal growth of divided cutaneous nerves. The most logical explanation is that it results from an invasion simultaneously of all parts of the graft by extensions from cutaneous nerves which invade the transplant along with the capillaries from the underlying bed. Recovery in those portions of grafts (Grafts Nos 4 and 10) not in contact with the usual satisfactory bed takes place from the margins as stated previously, for in these portions extension of nerve fibers from the underlying bed is impossible.

The time required for complete sensory regeneration in any given graft is

dependent upon several factors. The most important of these is the type of bed upon which the graft is placed. The earliest complete returns were seen in those cases where the grafts were placed upon areas denuded by the excision of thin superficial scars and which had relatively normal subcutaneous tissue beds (Grafts Nos 1, 2, 8, 12, 17 and 18). Normal sensation is usually present in such areas prior to operation but the fact that they are often surrounded by a similar type of scar does not seem to influence the rate of return. In those areas where dense, massive scars are encountered and excised, where the graft is placed directly on scar tissue, and completely surrounded by the same type of scar, the return is appreciably delayed. That complete regeneration can take place under such adverse conditions, however, is demonstrated by



FIG 4—Same as Fig 3. After excision of scars and replacement with split thickness grafts. Graft No 22 is seen in the forearm in which pain and touch sensations equaled that of normal skin at 203 days. Graft No 24, seen above the elbow, was followed only 70 days and was not yet equal to normal skin in either. The return occurred over all parts of both grafts simultaneously.

many of the cases of this series (Grafts Nos 9, 15, 21, 22, 25, 27, 30 and 32). In such areas, sensation is usually not normal prior to operation, and it has been interesting to note that grafts in these areas show a degree of return which is often far better than the sensation of the surrounding scar. This would be very difficult to explain if the regeneration in the graft were dependent on the longitudinal growth of divided cutaneous nerves. The fibers entering the graft would then have to traverse the scar proximal to it, and the sensation in the graft could hardly be expected to excel that of the surrounding area. With the fibers entering from the underlying bed, however, less resistance is encountered in the graft than in the scarred areas, and the degree of sensory regeneration in the former is definitely greater. Closely related to the type of bed as a factor in the rate of regeneration is the depth or severity of the primary burn or injury. Deep burns destroy cutaneous nerves and some of these never completely regenerate, especially if these areas are allowed to fill in with dense, extensive scarring. This is clearly demonstrated by Grafts

Nos. 41, 42, 43 and 44, in all of which complete anesthesia was still present after over four years. These four grafts were in the same individual, who had a complete loss of skin and subcutaneous tissue, and a partial loss of the underlying muscles as a result of a very deep burn. There was complete destruction of all cutaneous nerves in these areas, which have thus far failed to regenerate. Two pedicle flaps were also used in the same region in this case and they too showed no evidence of returning sensation after over four years. In this same individual, however, another split thickness graft was applied farther out on the arm where the burn was not so deep (Graft No. 45), and at the end of 52 months it showed complete return to both pain and touch, though neither was equal to normal skin. All of these areas were surrounded by normal skin with normal sensation, and had there been any regeneration of the destroyed cutaneous nerves, the margins of the grafts should have at least shown some evidence of return at the end of this time. It seems reasonable to conclude then that where some or all of the cutaneous nerves are left intact in the underlying bed, regeneration will take place over all parts of a split thickness graft simultaneously. In areas, however, where there is little or no overlap in the cutaneous nerve supply, as in the forehead, and the one incoming nerve is destroyed, sensory return can take place only with the regeneration of this nerve. In this and in any area where all cutaneous nerves are destroyed, and where there is no regeneration in these nerves, complete anesthesia will persist regardless of the type of graft used. Another factor closely related to the type of bed and the degree of the primary burn is the depth of the dissection necessary before the application of the transplant. In cases where contractures of the knee (Graft No. 34), and contracture of the axilla (Graft No. 29) are released, it is often necessary to place the transplant directly upon muscles. In these, complete return is always greatly delayed, but can still occur over all parts of the graft simultaneously unless all of the underlying cutaneous nerves are destroyed.

Another factor in the rate of regeneration, but least important of all, is the anatomic location of the graft. Certain regions of the body, particularly the lips, have a more abundant cutaneous nerve supply and in some instances (Graft Nos. 17 and 18), this seems to alter somewhat the rate of regeneration. The size of the graft used has been shown repeatedly to have no influence on the rate of sensory return. Graft No. 11, measuring eight inches in length and two and one-half inches in width, showed complete return to both pain and touch and was equal to normal skin at the end of 45 days. A much smaller graft (Graft No. 20), three inches long and one and three-quarters inches wide, did not show regeneration equal to that of normal skin until after 90 days. The former graft was placed upon an excellent subcutaneous tissue bed, while the latter was placed upon the donor area of a pedicle flap in which the full thickness of skin and most of the subcutaneous tissue had been removed. If, however, the return of sensation was dependent solely on the longitudinal growth of divided cutaneous nerves, the smaller graft should have shown com-

TABLE I

SYNOPSIS OF 45 CASES UPON WHOM SPLIT THICKNESS GRAFTS WERE APPLIED

Graft No , Case No , Age	Location of Graft	Per centage of Take	Size of Graft Inches	Type of Defect	Complete Return		Equal to Normal Skin
					To Pain	To Touch	
1 (K 47) 14 yrs	Forehead	100	6½ x 2¼	Old burn Very thin super- ficial scar	8 days	10 days	26 days
2 (K-47) 14 yrs	Neck	100	4 x 1½	Old burn Thin, superfi- cial scar contracture	7 days	9 days	28 days
3 (K 145) 13 yrs	Thigh	80	4 x 4½	Delayed application to donor area of recent thick pedicle flap	70 days First examination	70 days	322 days
4 (L 67) 10 yrs	Ankle	90	2¼ x 3	Old pressureslough Super ficial scar contracture	5 days	16 days	55 days
5 (L 29) 8 yrs	Abdomen	100	1½ x 2½	Delayed application to donor area of recent thin pedicle flap	12 days	22 days	55 days
6 (L-26) 8 yrs	Abdomen	85	4 x 2½	Delayed application to donor area of recent thin pedicle flap	7 days	14 days	52 days
7 (M 25) 8 yrs	Foot (dorsum)	90	4½ x 3½	Old burn Scar of mod- erate density	20 days	24 days	60 days
8 (K 195) 15 yrs	Thigh	100	6 x 3	Immediate application to donor area of full thick- ness graft	7 days	7 days	30 days
9 (I 18) 7 yrs	Palm and ring finger	95	2½ x 1½-1¾	Old rope burn Dense scar contracture	6 days	6 days	130 days
10 (L-175) 7 yrs	Flexor surface ring and middle fingers	100	1½ x 1½ (each)	Old rope burn Portion in ring finger laid on ex- posed tendon	7 days (40 days over ex- posed tendon)	7 days (40 days over ex- posed tendon)	22 days (110 days over ex- posed tendon)
11 (L-229) 5 yrs	Forearm and hand	100	8 x 2½	Old burn Scar of moderate density	12 days	15 days	45 days
12 (K-47) 14 yrs	Hand (dorsum)	100	3½ x 3¼	Old burn Thin superfi- cial scar	5 days	9 days	28 days
13 (L 39) 14 yrs	Neck	80	3 x 2	Delayed application to donor area of recent pedicle flap	8 days	12 days	55 days
14 (L-39) 14 yrs	Mastoid process	100	2 x 1½	Delayed application to donor area of recent pedicle flap	5 days	7 days	63 days
15 (L 39) 14 yrs	Hand (dorsum)	80	4 x 1½	Old burn Deep dense scar	10 days	21 days	95 days
16 (L 39) 14 yrs	Hand (dorsum)	95	3½ x 1¼	Old burn Deep dense scar	8 days	20 days	90 days
17 (L 39) 14 yrs	Lower lip	90	2¼ x 1½	Old burn Thin superficial scar	5 days	7 days	24 days
18 (L 39) 14 yrs	Upper lip	100	2½ x 1	Old burn Thin superficial scar	7 days	7 days	24 days
19 (L 39) 14 yrs	Hand and wrist (dorsum)	90	4 x 1½	Old burn Moderately dense scar	7 days	12 days	38 days
20 (L 39) 14 yrs	Neck	90	3 x 1¾	Delayed application to donor area of recent pedicle flap	13 days	21 days	90 days
21 (L 152) 12 yrs	Elbow (flexor surface)	90	6 x 1	Old burn Dense scar re- quiring deep dissection	6 days	9 days	278 days
22 (L 152) 12 yrs	Forearm and wrist (volar sur- face)	95	9 x 2½	Old burn Dense scar re- quiring deep dissection	7 days	10 days	203 days

TABLE I—*Continued*

Graft No , Case No , Age	Location of Graft	Per centage of Take	Size of Graft Inches	Type of Defect	Complete Return		Equal to Normal Skin
					To Pain	To Touch	
3 (L 152) 12 yrs	Forearm (dorsum)	100	6 x 2½	Old burn Dense scar re quiring deep dissection	6 days	11 days	Incomplete at 153 days
24 (L 152) 12 yrs	Arm (posterior aspect)	100	10 x 2	Old burn with dense scar	10 days	25 days	Incomplete at 70 days
25 (L-195) 7 yrs	Arm	90	5 x 4	Old burn Extensive de fect from release of axil lary contracture	6 days	9 days	128 days
26 (K 97) 10 yrs	Elbow	100	3½ x 3	Defect from full thickness loss of skin in a clothes wringer	10 days	25 days	45 days
27 (L 195) 7 yrs	Chest wall	100	6½ x 5	Old burn Extensive de fect from release of axil lary contracture	8 days	10 days	128 days
28 (L 195) 7 yrs	Forearm	100	6 x 2	Old burn Scar of moder ate density	7 days	7 days	97 days
29 (L 195) 7 yrs	Axilla	90	5 x 2½	Old burn Defect from re lease of axillary contrac ture	7 days	9 days	112 days
30 (J 82) 9 yrs	Chest wall	95	7 x 2	Old burn Dense scar con tracture	8 days	10 days	153 days
31 (J 82) 9 yrs	Shoulder (left)	100	6 x 3	Old burn Dense scar con tracture	7 days	7 days	120 days
32 (J 82) 9 yrs	Shoulder (right)	100	6 x 3	Old burn Dense scar con tracture	7 days	10 days	136 days
33 (L-196) 10 yrs	Lower lip	80	2½ x 1½	Old burn Scar of moderate density	6 days	6 days	55 days
34 (M 134) 13 yrs	Popliteal space	80	6 x 5	Old burn Dense scar with secondary flexion de formity	15 days	At 87 days, still none to to touch	
35 (M 134) 13 yrs	Leg	95	9 x 5	Open wound from deep burn 2½ yrs old	30 days	At 125 days, still none to touch	
36 (N-17) 13 yrs	Leg	98	8 x 2	Immediate application to donor area of pedicle flap	34 days	Incomplete at 155 days	
37 (I 53) 11 yrs	Abdomen	100	9 x 5	Old burn Dense scar with graft placed on muscles	At 125 days, partial return to pain None to touch		
38 (L 94) 10 yrs	Abdomen	100	4½ x 3	Old burn Thin superficial scar	First tests at 148 days and both pain and touch were equal to normal skin		
39 (I 83) 14 yrs	Abdomen	100	6 x 4	Old burn Dense scar con tracture	First examination at 330 days showed both pain and touch complete and equal to normal skin		
40 (I 83) 14 yrs	Neck	100	4 x 2	Old burn Scar of moderate density			
41 (I-53) 11 yrs	Axilla	95	6 x 6				
42 (I-53) 11 yrs	Axilla	90	4 x 2	Recent deep burn with full thickness loss of skin and subcutaneous tissue and part of underlying muscles	After 52 mos., there was complete anesthesia		
43 (I 53) 11 yrs	Elbow	90	2 x 2				
44 (I 53) 11 yrs	Abdomen	100	8 x 6				
45 (I-53) 11 yrs	Forearm	95	2 x 2½	Recent deep burn, but not as deep as the above four	At 52 mos., showed complete return to both pain and touch, almost equal to normal skin		

plete regeneration much sooner than the larger, irrespective of the type of bed available

In those grafts where some secondary scar contracture develops, the return of sensation may be delayed. This contracture is usually not primary in the

graft itself, but is instead located in the underlying bed with the result that the graft is piled up in small folds on the surface. These folds obviously increase the distance between parts of the transplant and the underlying bed and the rate of invasion of nerve fibers is proportionately decreased.

Free Full Thickness Grafts—The rate of sensory regeneration in eight free full thickness grafts which were studied was, in general, slower than the regeneration in split thickness grafts. This complete return, however, was found in all cases to be more rapid than that found by previous investigators. All, with one exception, showed regeneration over all parts of the graft simultaneously in both pain and touch, the degree of which progressed gradually to equal the sensation of normal skin. Only one (Graft No. 2), showed evidence of return from the proximal and lateral margins of the graft. This one exception agrees with the findings of previous investigators but the other cases were followed so closely that there can be no doubt that regeneration in all occurred over the entire graft simultaneously. This was a very deep burn with secondary scar contracture and it may be that most or all of the cutaneous nerves were originally destroyed and the ones which had regenerated in the scar were removed with its excision and the preparation of the bed. In one (Graft No. 6), there was evidence of hyperesthesia at the end of two weeks, but this rapidly disappeared and return to pain was noticed again at 26 days. In all other grafts, the return was slowly progressive from the time of first appearance until it had equaled the sensation of normal skin. The temporal dissociation in the return of pain and touch in full thickness grafts was much greater than that seen in split thickness grafts.

The factors influencing the rate of sensory return in this type of graft are

TABLE II

SYNOPSIS OF LIGHT CASES UPON WHOM FREE FULL THICKNESS GRAFTS WERE APPLIED

Graft No. Case No., Age	Location of Graft	Per centage of Take	Size of Graft (Inches)	Type of Defect	Complete Return		Equal to Normal Skin
					To Pain	To Touch	
1 (K-195) 15 yrs	Neck	100	1½ x 1¾	Old burn. Dense keloid scar but freely movable	25 days	36 days	52 days
2 (J-82) 9 yrs	Neck	100	5 x 2	Old burn. Dense scar with secondary contracture	22 days	56 days	180 days
3 (K-195) 15 yrs	Face	95	5 x 1¾	Old burn. Dense keloid scar but freely movable	14 days	22 days	56 days
4 (K-47) 14 yrs	Neck	100	5 x 2½	Old burn. Scar of moderate density with secondary contracture	27 days	45 days	65 days
5 (K-195) 15 yrs	Face	100	3¾ x 1¾	Old burn. Dense keloid scar which was freely movable	15 days	20 days	50 days
6 (K-170) 8 yrs	Face	90	1¼ x 2	Old burn. Dense keloid scar	26 days	49 days	62 days
7 (M-193) 12 yrs	Neck	100	6 x 1½	Old burn. Mild, relatively thin scar	30 days	44 days	110 days
8 (L-94) 10 yrs	Neck	95	4½ x 3	Old burn. Moderately dense scar with secondary contracture	First examination made at 148 days, at which time both pain and touch were com- plete and equal to normal skin		

identical with those described previously for split thickness grafts. All eight of these transplants were placed on excellent soft tissue beds with the exception of Graft No. 2, where extensive scarring was encountered and the transplant was made directly upon scar tissue. As a result, a much longer period of time was required for the sensation in this transplant to equal that of normal skin. The size of the graft used apparently was not a factor in the rate of regeneration.

Pedicle Flaps—Five pedicle flaps have been studied, but only three of these have been followed closely from the actual date of transplant. Of these three, two were transplanted to the dorsum of the hand and the third to the posterior and medial aspect of the heel. The results compared favorably to those reported by previous investigators using similar types of grafts. The return of

sensation was always noticed first along the proximal margin and along the margin which was attached at the time of the first stage of the operation. It then progressed distally and laterally across the body of the graft. Return to pain always occurred first and progressed far in advance of touch. There was no evidence of sensory regeneration in the body of the graft, independent of the progression from the proximal and lateral margins, similar to that seen so commonly in split and free full thickness grafts. All flaps in this series consisted of the full thickness of skin and subcutaneous tissue, and it is possible that extensions of nerve fibers from the underlying bed were unable to penetrate this mass of tissue. This could account for the difference in the type of return seen in pedicle flaps as compared with the thinner transplants.



FIG. 5.—(Grafts Nos. 1 and 5, Table II). Two full thickness grafts placed on excellent subcutaneous tissue beds in which both pain and touch were equal to that of normal skin at 52 and 50 days respectively. Return of sensation occurred over all parts of these grafts simultaneously.

The length of time required for the sensation in these three pedicle flaps to equal that of normal skin was much greater than that generally seen in the other two types. Complete regeneration in these grafts did occur, and this was undoubtedly aided by the fact that all were surrounded by normal skin and showed little or no evidence of scarring about their margins. The other two transplants were used in the axilla of a patient (Grafts Nos. 4 and 5), who had suffered a very deep burn with apparently complete loss of all cutaneous nerves in the region. As a result, total anesthesia still existed in both flaps 52 months later. This is the same case (Grafts Nos. 41, 42, 43, 44 and 45) which showed complete anesthesia in several split thickness grafts four years after operation.

TABLE III

SYNOPSIS OF FIVE CASES UPON WHOM PEDICLE FLAPS WERE APPLIED

Graft No., Case No., Age	Location of Graft	Per- centage of Take	Size of Graft (Inches)	Type of Defect	Complete Return		Equal to Normal Skin
					To Pain	To Touch	
1 (L-29) 8 yrs	Hand and wrist (dorsum)	100	5 x 4	Deep scar contracture, secondary to old tenosynovitis	83 days	125 days	240 days
2 (L-26) 8 yrs	Hand (dorsum)	100	3½ x 2¼	Scar contracture, secondary to injury and old osteomyelitis	65 days	95 days	218 days
3 (K-145) 13 yrs	Heel	100	3½ x 3	Early flap for covering com- pletely denuded posteromedial aspect of os calcis	124 days	158 days	396 days
4 (I-53) 11 yrs	Axilla	100	2 x 1½	Neighboring flap shifted for cov- ering defect resulting from burn	First checked 52 mos later at which time there was still com- plete anesthesia in all parts of the graft		
5 (I-53) 11 yrs	Axilla	100	2½ x 1¼	Neighboring flap shifted for cov- ering defect resulting from burn			

SUMMARY

The return of pain and touch sensations has been closely followed in a series of split thickness grafts, free full thickness grafts, and pedicle flaps. This sensation was followed not only until complete return was present to both pain and touch but also until it equaled that of normal skin in other parts of the body. The results obtained are quite different from those obtained by previous investigators. It has been found that in split thickness grafts, the regeneration usually occurs over all parts of the graft simultaneously rather than by progression of the sensation from the proximal and lateral borders of the grafts as previously supposed. The only exception to this lies in those grafts which cannot be placed on a satisfactory soft tissue bed. The same holds true in the majority of free full thickness grafts, for only one in a series of eight transplants of this type showed evidence of regeneration first along the proximal and lateral margins, with progression distally over the remaining portion of the graft. The findings in pedicle flaps agree with previous reports, in that regeneration takes place first along the proximal border and the portion attached first, progressing distally slowly over the body of the graft. In none of the pedicle flaps was there any evidence of sensory return in the transplant independent of this progressive change. Complete recovery of sensation in all types of grafts is possible to an equal degree, unless the cutaneous nerves of the involved region have been completely destroyed at the time of the original burn or injury, and have failed to regenerate.

Previous reports have agreed that the regeneration of sensation in any graft was directly proportional to the thickness of the graft used. In this series, the exact opposite has been found. Generally speaking, and other things being equal, regeneration is more rapid in split thickness grafts than in any other type. Next in order is the free full thickness graft, and slowest of all is the pedicle flap. In other words, the rate of return is inversely proportional to the thickness of the graft used in the three types which were studied. A temporal dissociation in the recovery of pain and touch has been demonstrable in all

types, but this becomes more pronounced as the thickness of the graft is increased

I wish to express my appreciation to Dr J B Brown for the use of his cases in the conduct of this investigation

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ERRATUM

Page 34, 21st line, of the January 1938 issue should read 140° C instead of 140° F

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GELATINOUS MAMMARY CANCER

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ALTHOUGH rare, gelatinous cancer was among the first of the several varieties of mammary carcinoma to be described as a separate and distinct form. Its syrupy, jelly-like characteristics in the gross, and the peculiar ground substance under the microscope, make it readily recognizable and have permitted accurate classification. Lange⁶ has credited Otto,⁹ in 1816, with the first description of gelatinous carcinoma. Robinson,¹¹ in reporting a case to the pathologic Society of London, in 1852, stated that only four similar tumors affecting the breast had been recorded, one by Jonathan Muller,⁸ one by Rokitsansky,¹² one in the London Hospital Museum, and one in St Thomas's Hospital.

The history of Robinson's case is of interest in that the patient remained free of the disease for five and one-half years after excision. He related that the patient, age 56 "was under the care of the late Mr Tyrell seven years ago (1827) for a tumor (not ulcerated) in the right breast, and another in the right armpit, both of which were removed by the knife and the wound healed perfectly in a month. About 18 months ago, a hardness was noticed on the termination of the wound towards the nipple. About one-third from the outer termination of the cicatrix is a small lobulated tubercle, which has existed four months, and which evidently increased. It is of purple colour, covered with crimson vessels, and surrounded by a similar stony induration, firmly attaching it to the chest.

"November 27, (1834) The ulcers had scarcely varied at all, the redness of the integuments of the right arm and the swelling somewhat subsided, but the hardness and tenseness continued. She had a troublesome cough, wheezing, dyspnoea and sense of weight in the chest, with great emaciation, and although relieved by blistering, expectorants, hyoscyamus, and mild tonics, she died in the evening from effusion into the chest. At autopsy the tumors in the course of the cicatrix had extended as far as the ribs, and implicated them. They were specimens of colloid cancer, and appeared much the same as during life, although not so vascular. One had a fibrous appearance, the other, a vascular, and into one of these blood had been effused. Upon incising it posteriorly, the gelatiniform appearance was beautifully

shown The lungs were congested, and the an-cells somewhat dilated, but they were not at all affected by malignant disease There was about a pint of serous fluid in each side of the chest The heart was healthy The other viscera were not examined "

Gaabe,³ in 1908, found that this type of cancer was twice as curable as the ordinary form Halsted,⁴ in 1915, described a peculiar sensation on palpation which he thought was diagnostic of the gelatinous cancer He stated that the tactile impression "might be defined as a delicate swish or crush of a jelly-like structure under tension" Lee, Hauser and Pack⁷ reviewed the

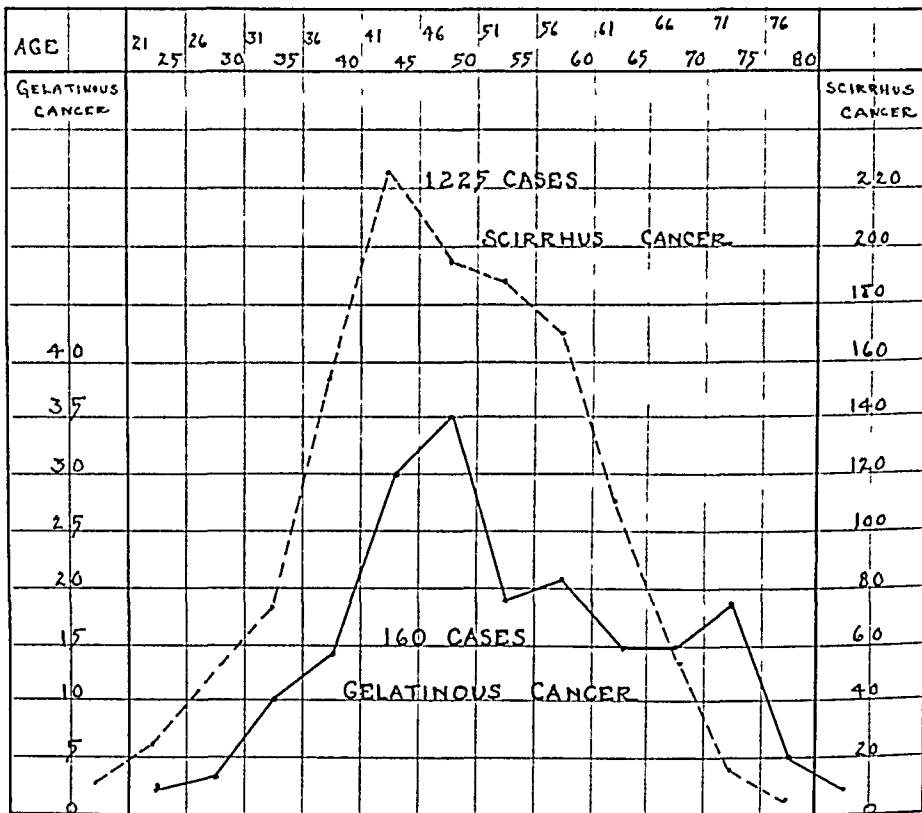


CHART 1 —Shows the comprison of the age incidence of 1,225 cases of scirrhus cancer with 160 cases of gelatinous cancer (including the author's series and those collected by Grrbe)

literature on the subject, in 1934, and found the incidence given by various authois as 1 to 2 per cent of all cancers of the breast They reported 30 cases, recorded in the Memorial Hospital, with 57 per cent of five-year cures

The present study is based upon 83 cases of gelatinous carcinoma recorded among a total of 2,300 cancers of the breast in the Surgical Pathological Laboratory This study emphasizes the slow growth of these tumors, their low degree of malignancy and their tendency to local recurrence five to 30 years after treatment by radical operation

Clinical Features —Gelatinous carcinoma occurs on the average in more elderly patients than ordinary mammary cancer One-third of the cases in the present series occurred between the ages of 41 and 50 and nearly an equal number occurred in patients between the ages of 60 and 79 The peak of the age incidence was between 46 and 50 years compared to a peak between

41 and 45 years for ordinary cancer of the breast (Chart 1) The average age in the series of Lee, Hauser and Pack was 52 years

A discovery of a lump in the breast was the first sign noted by the patient in 80 per cent of our cases The painless character of the lump and its slow growth enhance the natural period of delay in consulting a physician for treatment In 33 cases, the lump was known to be present for a year or more before the first examination and in nine of these cases, the duration of the lump was five years or longer In 36 cases, the duration of the lump was less than a year, the average duration in this group being 41 months compared to 43 years for the group in which the duration of symptoms was a year or more In three instances the lump was discovered during routine examination, the patient being unaware of its presence One patient had noticed hardness of the affected breast for 20 years, the hardness apparently disappeared for several years but recurred eight years before admission and rapidly increased in the past year During the past three years she had had a sanguineous discharge from the nipple When examined in 1915, there was diffuse induration of the entire breast with a soft fluctuating mass 3 cm in diameter beneath the nipple This patient died six years after radical operation with invasion of the mediastinum

Gaabe has estimated (on the basis of 88 cases collected from the literature) that the duration of symptoms in gelatinous carcinoma is two and one-half times that of the more common scirrhous form Lange, basing his conclusions on a series of breast cancers reported by various German authors, states that ulceration of the skin in scirrhous cancer occurs from one to two years after the onset of symptoms In the 75 cases of gelatinous carcinoma collected by him, the average period elapsing before fixation of the skin was 33.9 months and ulceration occurred after an average period of 57.7 months

The statement by patients, giving the duration of their tumor in terms of years, is corroborated by the similar period which has elapsed between local excision and the recurrence of a tumor of appreciable size in the scar In the case reported by Robinson, cited above, the first signs of local recurrence were five and one-half years after excision In a similar case, recorded in this laboratory, local excision was performed in October, 1919, for a tumor the size of a walnut, thought to be a retention cyst The recurrent tumor, which was half again as large, was noted in the breast in February, 1922 A simple amputation of the breast was performed, and, in November, 1930, an enlarged axillary lymph node was excised which showed mucoid cancer The patient was reported well in April, 1937 Halsted performed excisions for recurrent tumors, in 1903 and 1906, for a case which had had two previous excisions at four-year intervals This patient died in an automobile accident in 1931, at the age of 73

Lee, Hauser and Pack have emphasized the large size of some of these growths Lange found that the tumors varied in size from a walnut to that of an orange Only two of his cases were the size of a child's head Gaabe found that 10 per cent of 88 cases were of unusual size The present study

emphasizes the relatively small size of the tumor in comparison with the long duration of symptoms. The average size of the tumor in 58 cases was 5.3 cm., and approximately 50 per cent had a diameter of 4 cm. or less. There were only five tumors, 10 cm. or over in diameter, the largest, 22 cm., was a recurrence after local excision. Three cases had the diameter of 8 cm., and one, 9 cm. (Chart 2).

Beside its slow rate of growth, and the tendency for the tumor to occur near or after the menopause, there is very little additional information that

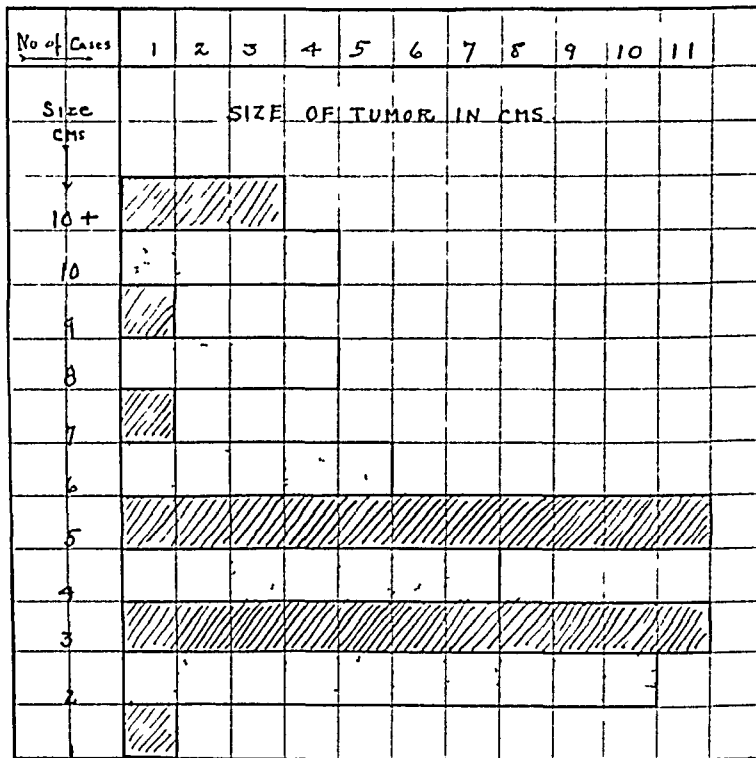


CHART 2—Shows the maximum diameter of the tumor in cases of gelatinous carcinoma

can be gleaned from the histories given by these patients. Pain is usually not an early symptom. Approximately 10 per cent of the patients noted a discharge from the nipple, usually of a sanguineous character, and an approximately equal number had noted change in the size or color of the nipple, with or without itching or irritation. The history of trauma or preceding lactation mastitis occurred in an insignificant number. Discoloration or ulceration of the skin prior to examination was noted in 14 cases. Where present, this was usually given as the reason for seeking advice. In general the skin changes were present only in those tumors which were six or more centimeters in diameter. There was one exception.

There are four chief findings on clinical examination which suggest a diagnosis of gelatinous carcinoma. The first is the relatively small size of the tumor in comparison with the long duration of symptoms. The second is the protrusion and enlargement of the nipple on the affected side. This finding of protrusion, rather than retraction, was noted by the examiner in eight cases in the present series and the finding is probably of more frequent occurrence, since its diagnostic importance in gelatinous carcinoma

has not been heretofore emphasized (Fig 1) The third is the cystic character of the growth on palpation The diagnosis of benign cyst was made prior to operation in 11 cases in the present series

The differentiation from a benign cyst should not be difficult in these cancers because the tumors are often larger (4 to 6 cm), and on aspiration do not yield the cloudy fluid obtained from a cyst of similar size They are accompanied by atrophy of the overlying fat The fourth diagnostic finding



FIG 1—Path No 60479 Gelatinous carcinoma occurring in a colored woman age 62. Note the bulging and enlargement of the nipple on the affected side Enlargement and protrusion of the nipple may be a diagnostic sign in these growths

in the present series, is the feeling of a "swish" on firm pressure, originally described by Halsted This impression of a ruptured cyst, or the finding of an area of fluctuation in an otherwise solid tumor are important in diagnosis

Gelatinous carcinoma occurs most frequently in the outer upper quadrant and in the central portions of the breast The upper inner quadrant, the lower outer quadrant, and the lower inner quadrant are affected in the order of frequency given The location of the tumors studied in the present series and those reported by Lee, Hauser and Pack and by Gaabe, are shown in Table I

TABLE I

LOCATION OF THE TUMOR IN 91 INSTANCES OF GELATINOUS CARCINOMATA

Author	Upper Outer Quadrant	Upper Inner Quadrant	Center	Lower Outer Quadrant	Lower Inner Quadrant	Entire
Author's series	11	8	16	5	1	4
Lee, Hauser and Pack	4	4	10	0	3	1
Gaabe	15	3	0	6	0	0
Totals	30	15	26	11	4	5

In seven of the cases in the present series, there were multiple tumors in the same breast, these were either in the outer or upper portions of the breast. In three cases both breasts were ultimately involved. In one, the involvement of the second breast occurred one year after the radical operation for the first tumor and was a mucoid cancer. In the second case, the involvement three years later showed a scirrhous cancer with mucoid change. In the third case, a similar tumor appeared beneath the nipple in the opposite breast and enlarged nodes were palpable in the axilla five years after radical operation. In the 75 cases studied by Lange, three developed cancer in the other breast. In one, the tumor in the second breast was a colloid cancer. The second was diagnosed as scirrhous and the third as Paget's disease.

Differential Diagnosis—While the diagnosis of gelatinous cancer is usually made on the gross specimen or the microscopic section, there are 11 cases in the present series in which the nature of the tumor was correctly inferred from the clinical findings. The relatively small size of the tumor in cases where the symptoms had been present several years and its encapsulated rounded character with a boggy or fluctuant feeling, together with atrophy of the overlying fat, dimpling, or palpable axillary lymph nodes, suggested the presence of mucoid carcinoma. In four of the five cases reported by Halsted, and included in this series, the impression of rupture of delicate membranes or "swish" led to a diagnosis of mucoid carcinoma.

As mentioned above, the tumor was incorrectly diagnosed as a benign cyst in 11 instances. In four cases, the impression was that of an intracanalicular myxoma. In an additional four cases, the diagnosis was benign intracystic papilloma or papillary carcinoma. In the remaining cases, where the diagnosis of gelatinous carcinoma was not made clinically, the clinical impression was that of ordinary mammary cancer. In the cases where the diagnosis of benign cyst was made, sufficient importance was not given to the nearness of the tumor to the skin, the atrophy of the overlying fat, its size, or its failure to yield a characteristic cloudy fluid on aspiration. The distinction between a giant intracanalicular myxoma, or degenerating fibroadenoma is more difficult. Usually the fibroadenomata of corresponding size are opaque on transillumination, whereas in gelatinous carcinoma if the lesion is soft and sufficiently gelatinous the tumor will transilluminate. If a large size (No. 18 gauge) needle is used for aspiration, the characteristic gelatinous material should be demonstrable (Fig. 2).

Papillary adenocarcinoma or benign intracystic papilloma may be simulated by these growths. A central location, a sanguineous discharge from the nipple, and a boggy feeling with or without areas of fluctuation, occur in both gelatinous and papillary cancer. That the differential diagnosis may be impossible clinically, is indicated by the pathologic finding of mucoid change in eight cases of papillary cancer recorded in this laboratory.

Gross Pathology—Careful study of the gross and microscopic pathology of mucoid carcinoma indicates that there are two groups of mammary cancers which contain this type of gelatinous material. In one group, the tumors

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contain a shiny, translucent gel throughout their substance, in the second group, the gelatinous change is found in one or more portions and solid, dense tissue in the remainder of the growth. In the present series, 59 tumors showed a characteristic gelatinous substance throughout, and 24 showed secondary mucoid change in cancers of the scirrhous or duct type.

The gross specimens of typical gelatinous cancer may be cystic or solid, encapsulated or nonencapsulated. The group of mammary cancer in which mucoid change is found in isolated portions of the gross specimen only, or under the microscope, have shown grossly a resemblance to scirrhous or duct cancer.



FIG 2—Path No 69609 Photomicrograph showing cancer cells in the mucoid material aspirated from a case of gelatinous carcinoma

In those of carcinoma with complete gelatinous change, 16 of the cases were described as encapsulated and two as circumscribed. The encapsulated tumors at exploration resemble a cyst or degenerated intracanalicular myxoma. In one instance, the cyst-like tumor presented a blue dome because of its vascularity. In another the tumor was polycystic. When the capsule of these cystic tumors is incised the soft, translucent jelly-like material, often flecked with hemorrhage, bulges or flows from the incision. The exuded material has frequently been compared to tapioca (Figs 3 and 4).

Encapsulated gelatinous carcinoma may closely resemble degenerating intracanalicular myxoma grossly. However, in the true myxomata the mucoid tissue is firm, and does not exude from the cut surface.

In the nonencapsulated gelatinous carcinomata, the mucoid material may invade the surrounding tissues, including fat and muscle, or the gelatinous

material may be diffuse throughout the more solid growth giving the cut surface a slimy, grayish cast or a honey-combed appearance (Figs 5 and 6) Three of the nonencapsulated tumors were fixed to the overlying skin and two had invaded the pectoralis muscle. In such solid nonencapsulated tumors, pockets of mucoid material such as are found in encapsulated tumors may occur (Fig 7)



FIG 3—Path No 24144 Photograph of a gross specimen showing the bulging dark jelly like material in a case of encapsulated gelatinous carcinoma



FIG 4—Path No 4874 Photograph of a gross specimen showing the encapsulated character of gelatinous growth which feels like a cyst when palpated

In six cases in the present series, gelatinous material was interspersed in tumors having the structure of papillary carcinoma grossly (Fig 8). This type of gelatinous carcinoma has been well described and illustrated by Lee, Hauser and Pack. In two other cases, the papillary carcinoma showed a typical structure and pockets of mucoid material were found in isolated portions of the tumor (Fig 9). More frequently, when only partial mucoid change is found, the tumor is a slowly growing scirrhous carcinoma of large size (Figs 10A and B).

Microscopic Pathology—Gelatinous change has been described in nearly all varieties of mammary cancer. In general, the more slowly growing forms

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of carcinoma of the breast are more prone to mucoid change, but this type of gelatinous material may be found in isolated portions of more malignant forms. In such cases the gel is apparently deposited in foci where interruption of blood supply, or other factors have interfered with growth. Gelatinous carcinoma therefore, can be divided microscopically into those cases



FIG 5—Path No 60479. Gelatinous carcinoma of solid character showing a characteristic glossy surface



FIG 6—Path No 17869. A solid gelatinous growth removed at operation for recurrence, 19 years after mastectomy for the primary tumor

in which the gelatinous material predominates throughout the entire tumor and cases in which the gelatinous material is deposited in isolated foci or sparsely through solid tumor growth. The majority of gelatinous carcinomata contain epithelium with definitely malignant features, resembling that found in



FIG 7—Path No 29697 A specimen of gelatinous carcinoma combining cystic and solid features

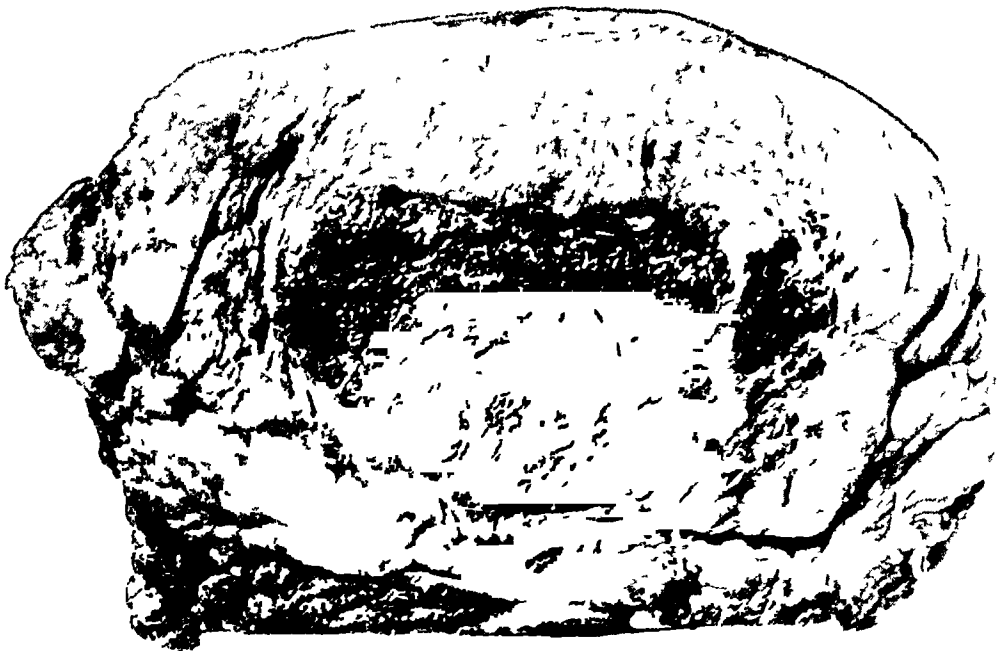


FIG 8—Path No 9733 A specimen showing mucoid change in a papillary carcinoma (so called bulky cystadenocarcinoma)

ordinary scirrhous or papillary cancer, whether or not the mucoid substance is diffuse and abundant or scarce (Fig 11)

Where the cancer cells resemble those found in ordinary scirrhous carcinoma, the degree of malignancy and the prognosis vary with the amount of mucoid substance found. This is in contrast to the view of Cheate and Cutler,¹ who stated that the clinical course does not depend upon either the presence or the extent of the gelatinous degeneration. In the present series, there were 58 cases with malignant epithelium of the scirrhous type. In 34 of these cases, the gelatinous change was diffuse throughout the tumor and the percentage of five-year cures was 54. In 24 cases, mucoid change appeared in isolated portions of the growth or was exceedingly scarce. In

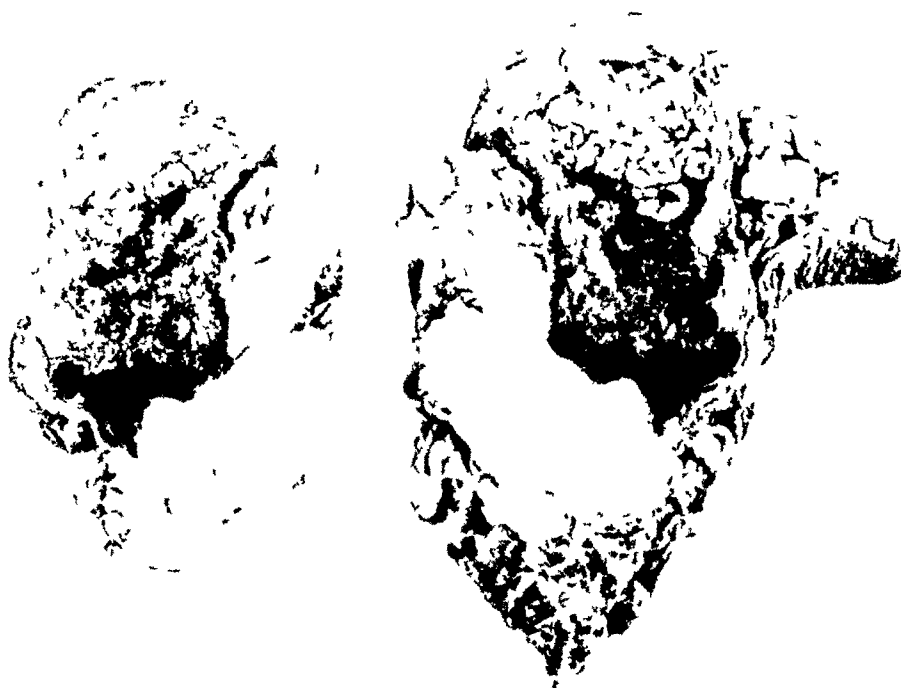


FIG 9—Path No 50573. Papillary carcinoma showing mucoid change. The papillary structure is seen at the upper margin of the growth and the gray gelatinous material at the lower. There is an intervening dark zone of hemorrhage.

this latter group, there were 30 per cent of five-year cures, a percentage of survivals which was identical with that found in 1,225 cases of ordinary scirrhous carcinoma recorded in this laboratory.

Among the carcinomata of the breast in which gelatinous material predominates, there is a third group of cases containing epithelium of the basal cell type. Judging from the relatively benign character of the epithelium and from the large amount of mucoid substance, the prognosis in these growths should be unusually good. This assumption is borne out by the cases of this character in this series. Nineteen of 25 cases were traced and, with the exception of three dying from other causes, all survived the five-year period (100 per cent of five-year cures).

Among those gelatinous carcinomata with cells approaching the basal cell type, there is a group which is microscopically indistinguishable from basal cell cancer of the adenocystic type, such as is found in the parotid gland,



B

FIGS 10A and B—Path Nos 10639 and 7567 Gross specimens of slowly growing scirrhous carcinoma with areas of gelatinous degeneration

TABLE II

AN ANALYSIS OF THE FIVE-YEAR MORTALITY RATE BASED UPON THE TYPE OF CASE

Type of Cancer	No of Cases	Not Traced	Dead Within 5 Years	Dead Other Causes	Dead After 5 Years	Well Over 5 Years	Per Cent 5-Year Cures
Basal cell cancer, with complete mucoid change	25	6	0	3*	3	13	100
Papillary or scirrhous cancer, with complete mucoid change	34	8	11	2	4	9	54
Scirrhous cancer, with partial mucoid change	24	4	13	1	3	3	30

* One of these patients died postoperatively

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and a portion of the growth may resemble benign mixed tumors of the parotid (Fig 12) That typical mucoid carcinoma of the mammary gland may originate as a form of adenocystic basal cell cancer, is suggested by three cancers of the breast, recorded below, in which the mucoid change at operation was not yet pronounced and the predominating structure was adenocystic basal cell cancer

Path No 56134—This case was referred to the laboratory by Dr Louisa A Keasbey of Lancaster, Pa The patient is a white female, age 46 There is a small lump in the right breast which was noted for one year The patient has had three normal pregnancies, the last 23 years ago She still menstruates regularly There are no other

FIG 11



FIG 12

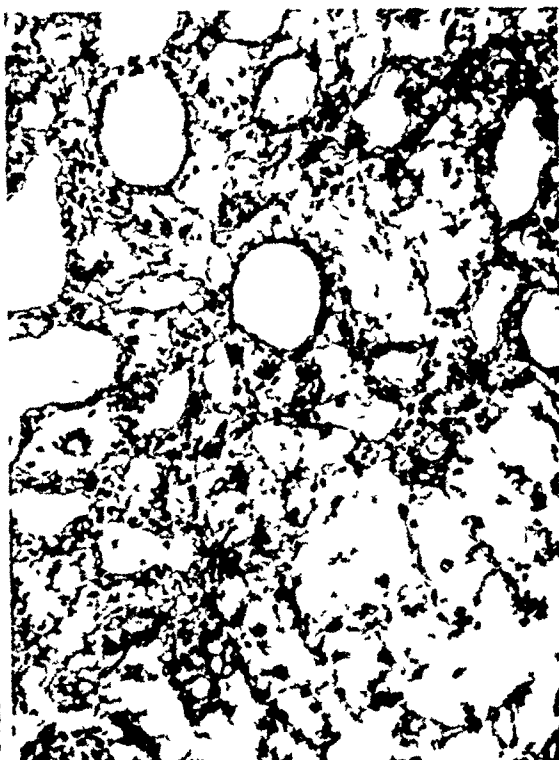


FIG 11—Path No 41029 Photomicrograph of scirrhous carcinoma with mucoid change The majority of gelatinous carcinomas show cancer cells of this type but with more abundant gelatinous material

FIG 12—Path No 27946 Photomicrograph of a gelatinous carcinoma resembling a mixed tumor of the parotid gland This patient remained well 14 years following radical operation

abnormalities in either breast The tumor, which is well circumscribed and situated deeply in the breast tissue, is 3.5 cm in diameter A radical mastectomy was performed in February, 1935 The tumor was definitely circumscribed and contained one small cyst, 0.5 cm in diameter

Microscopically, the tumor has the appearance of adenocystic basal cell cancer There are numerous acini of variable size containing a mucoid secretion (Fig 13) The patient was reported well in September, 1937

Path No 35154—The patient was a woman, age 44 The tumor, 2 cm in diameter, was not adherent to the skin or deep structures, and was situated in the left breast There were no palpable nodes in the axilla The upper half of the breast only was removed down to the pectoral muscle in April, 1924 Dr Bloodgood reported on the section as probable low grade carcinoma and classified it as borderline but recommended that it be treated as cancer (Fig 14) The patient was given instead post-operative irradiation In December, 1924, she had had a goiter operation, additional roentgenotherapy, and nodules were palpable in the other breast There is no note of additional therapy and the patient was reported apparently well, May 12, 1930

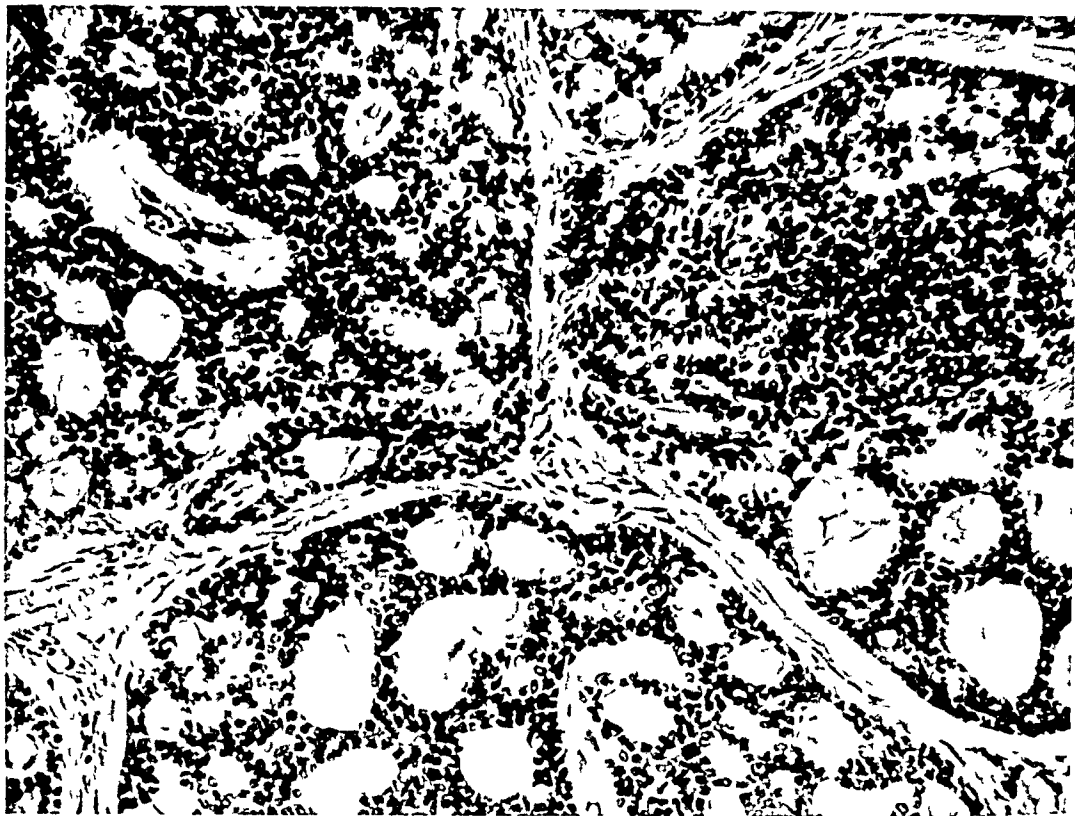


FIG 13—Path No 56134 Photomicrograph of an adenocystic basal cell carcinoma of the breast with areas of mucoid secretion (case of Dr I. A. Kershev, Lancaster, Pa.)

FIG 14

FIG 15

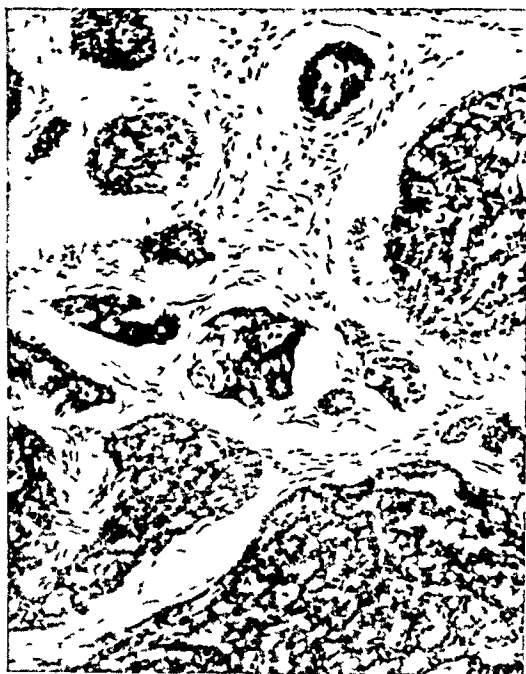


FIG 14—Path No 35154 Photomicrograph of an adenocystic basal cell carcinoma of the breast. The tumor was treated by excision and postoperative irradiation. The patient has remained well six years.

FIG 15—Path No 39095 Photomicrograph of a basal cell cancer of the breast containing tissue suggestive of benign adenoma of the parotid gland. Note the dilated acini with mucoid secretion.

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Path No 39095—The patient is a white woman, age 46, who had a tumor excised from her breast elsewhere. The specimen contains an encapsulated tumor mass 5 cm in diameter. The capsule is intact at every point and the mass is embedded in fat. The tumor has a soft and spongy feeling and on section it is a slate-black color. The gross diagnosis suggests hemangioma.

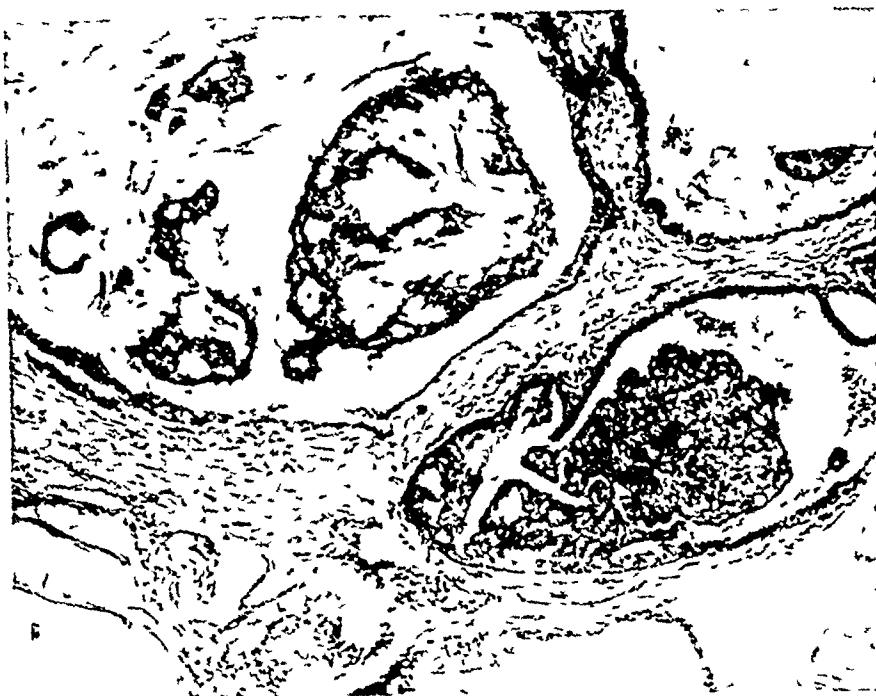


FIG 16—Path No 35024. Photomicrographs of a small papillary tumor of the breast undergoing mucoid change. The patient, age 30, had two small tumors about 1 cm in diameter, one near the right and one near the left nipple. The nodules were treated by simple excision. The patient has remained well 14 years without further treatment. This case illustrates the origin of mucoid carcinoma from papillary tumor and the low degree of malignancy of such tumors in their early stage of development.

The section of the tumor shows strands of basal cells which differentiate toward cuboidal cells, forming definite acini enclosing large amounts of colloid-like material (Fig 15). The coagulated material extends into the stroma and many of the acini are

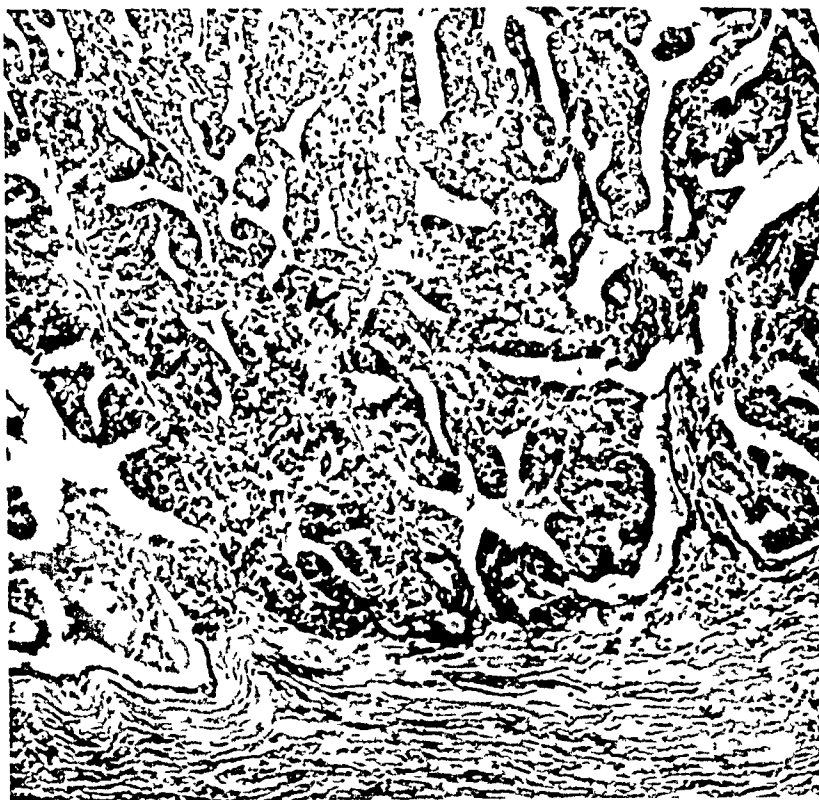


FIG 17—Path No 50507 Photomicrographs of a papillary carcinoma with mucoid change. This patient was operated upon four times, over a period of 30 years. She has remained well six years since the last operation. The upper picture shows the papillary structure and the lower the gelatinous portion.

ruptured. The tumor has a definite fibrous capsule, the surrounding lobules of breast are atrophic and embedded in loose periductal fibrous tissue which stains poorly. At one point in the surrounding breast tissue bordering on the tumor there is a duct adenoma. None of the tumor cells have a definitely malignant appearance, although there is a moderate variation in the size and density of the nuclei.

Mammary carcinoma with large amounts of gelatinous material infiltrating the entire tumor may contain islands of tumor cells suggesting an origin from slowly growing scirrhous or papillary cancer. Such tumors contain small alveolar structures with malignant cuboidal cells surrounded by a characteristic gel, encased in the remnants of periductal or perilobular connective tissue. Such slowly growing adenocarcinomata may contain portions indicating an origin from benign or malignant papillomata (Fig 16). More often the relation to papillary carcinoma is indicated by the gross specimen (Figs 10 and 11). Three cases of papillary carcinoma with partial mucoid change have been excluded from the present series because of relative insignificant amounts of mucoid material. In the following case mucoid change predominated in the recurrent tumors.

Case Report—Path No 50507. The patient at the age of 18, in 1902, had a benign papilloma removed from the right breast with a good margin of breast tissue. Her first pregnancy was at the age of 27, during the next six years she had four more children. There were recurrent swellings in the right axillary region with each pregnancy which spontaneously regressed during lactation.

Eight years after the birth of her last child and 23 years after the first operation, at the age of 41, a small nodule appeared in the scar. This nodule gradually enlarged, the overlying skin showed a purple discoloration, broke down, and discharged a dark, bloody fluid. At a second operation, in 1925, this mass, which proved to be a papillary carcinoma, was removed and a dissection of the nodes of the right axilla performed. Four years after the second operation, nodules appeared in the scar in the region of the axillary prolongation of the incision. These enlarged slowly and became tender during the next two years. At the age of 47, in November, 1931, 29 years after the first excision, a third operation was performed and the recurrent masses removed. At this operation gelatinous material flowed from the wound. During the next ten months additional masses appeared in the right axilla and a fourth excision was performed in October, 1932. The patient was reported well five and one-half years later, in April, 1938.

The tissue from the first operation was reported as a benign intracystic papilloma. That from the three subsequent operations showed papillary carcinoma with mucoid degeneration (Figs 9 and 17).

In most of the cases recorded in this series, a form of scirrhous carcinoma with a tendency to differentiate alveolar-like structures was apparently a starting point of the gelatinous tumor. The more definite the alveolar-like structures the greater tendency to mucoid change. Where the histology approached typical scirrhous carcinoma, the amounts of gelatinous material were small or were found only in isolated portions of the tumor.

Origin of the Gel—The present study indicates that a variety of mammary carcinomata may undergo mucoid changes, resulting in typical gelatinous carcinoma. Slowly growing scirrhous cancer, papillary adenocarcinoma,

and adenocystic basal cell cancer are the most frequent sources for growths in which the characteristic gelatinous material pervades the entire tumor structure. Kaufman,⁷ Lange⁸ and Ewing² are among those authors who have sought to trace the origin of the gelatinous material to stromal degeneration. The abundance of the gel and the crowding out of epithelial elements in some of these growths favors such an interpretation (Fig 18). The gelatinous material, moreover, does not take the specific stains for mucin. Ribbert,¹⁰ Gaabe,³ and most recent contributions hold that the gel results from the secretory ac-

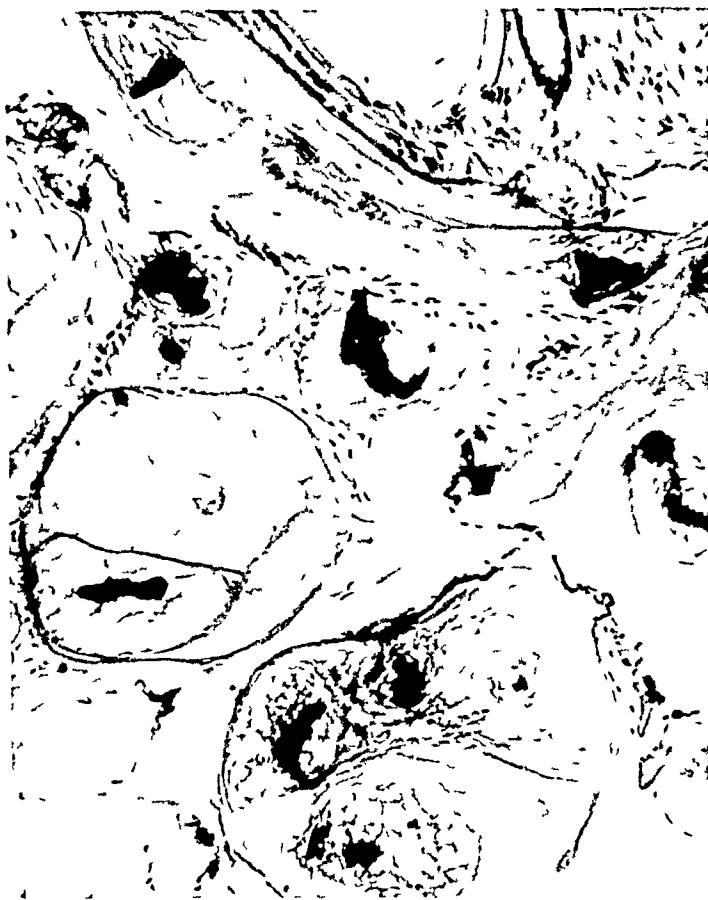


FIG 18—Path No 18441 Photomicrograph of gelatinous carcinoma where the mucoid change is crowding out the epithelial elements which resemble basal cells

tivity of the malignant epithelium. There is a preponderance of evidence in support of such a view. The occurrence of the gel in metastatic deposits in the lung and lymph nodes, where fat and fibrous material are sparse or absent, indicates an epithelial origin (Fig 19). Moreover, in papillary tumors and adenocystic basal cell cancers of the breast undergoing mucoid change the gel can be seen forming within the acinar structures of the tumor away from stromal elements (Figs 12 and 13).

Treatment—A study of the results of treatment in gelatinous carcinoma emphasizes the tendency to late recurrence and a long survival period, in spite of incomplete or unsuccessful surgery. A period of 5 to 10 years of freedom

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from symptoms following treatment does not necessarily indicate permanent cure. In the present series, there were 14 cases who suffered late recurrences. Three patients died in the sixth year following radical surgery, two in the seventh, one in the eighth year, and one in the tenth, and another had a similar cancer in the opposite breast after five years. Two patients died of

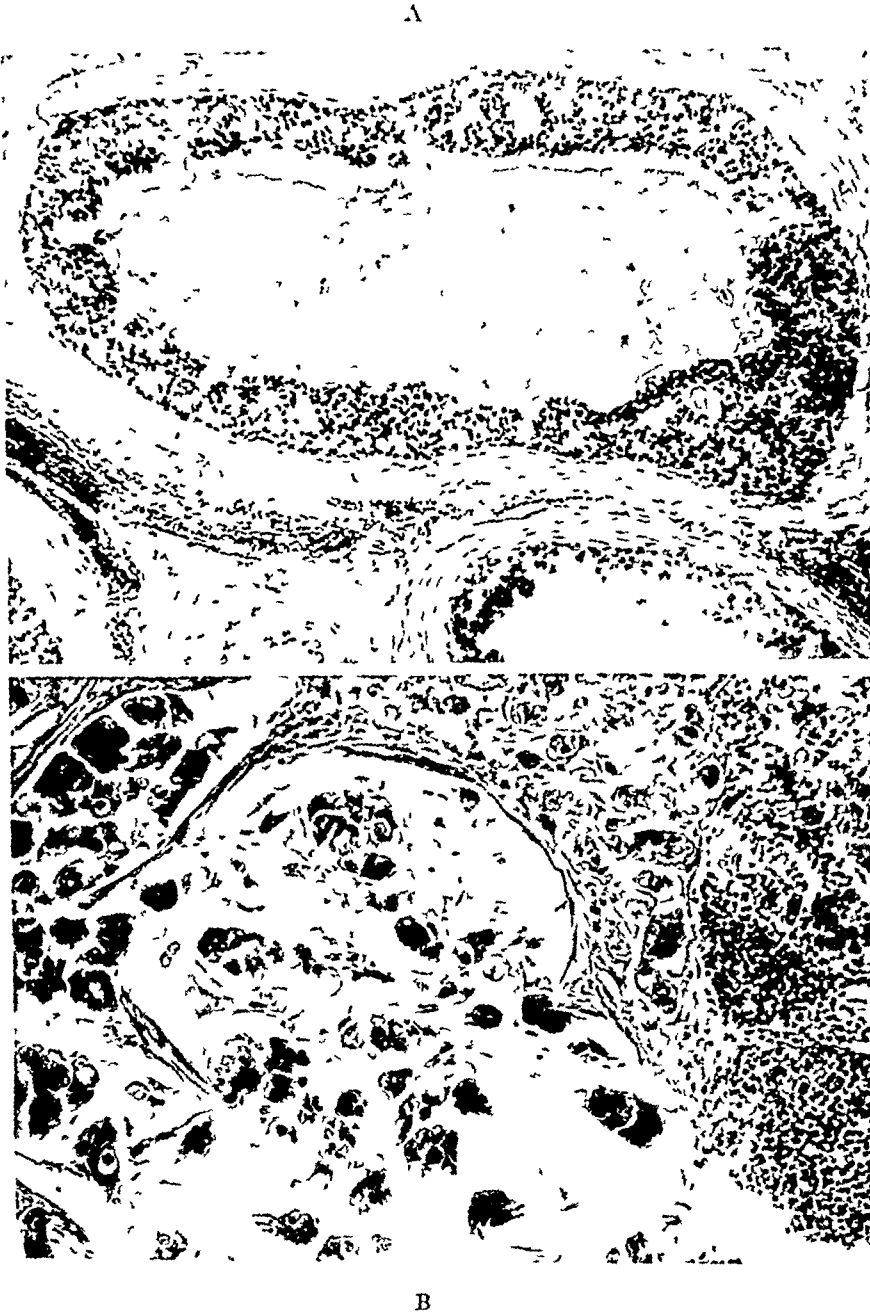


FIG 19 A and B—Path No 8030 Photomicrograph of comedo carcinoma in which gelatinous change occurred in the metastatic nodules of the lymph node but not in the primary growth. Above is illustrated the structure of the primary growth, below cancer cells with mucoid secretion in the metastasis to the lymph node.

metastases, 16 and 18 years, respectively, after the complete operation, and a third had metastases 14 years later. Two patients had repeated excisions for the disease over a period of 11 years, one remaining well eight and the other 25 years after the last operation. Another patient had three operations

in seven years and is well six years after the last excision. In all, 14 patients survived the last treatment by 11 or more years, and among these 11 have remained well.

Of 83 gelatinous cancers, 65 have been adequately traced and of these 40 or 61 per cent survived the five-year period, the remaining 25 dying of the disease. If the cases with diffuse gelatinous change, discovered only after microscopic study, are included, there are 76 per cent of five-year cures, and if among these only, those showing basal cells are considered, the five-year survivals are 100 per cent.

In 19 cases, the initial treatment was excision only, in one no treatment was given, and in five cases simple mastectomy was performed. In 12 of the 19 cases, where excision was employed, the radical operation was performed in the next few days. The remaining cases were treated by further partial operations (simple mastectomy and excisions) or by deep roentgenotherapy. In five cases, simple mastectomy was the initial treatment, followed by further surgery in only one instance.

No cures were established by simple excision alone with the exception of the case illustrated in Fig. 16. One case treated in addition by deep roentgenotherapy is living six years. One case was treated by excision in 1919, by simple mastectomy in 1922, and by excision of diseased axillary nodes in 1930, and is well in 1938. Another patient was treated by excision in 1895 and 1899, received further dissections by Halsted in 1903 and 1906, and died from accidental death in 1931. One patient treated by simple mastectomy was well 16 years later and another is well after six years. The history of two cases initially treated by incomplete operation who survived for more than 15 years, but eventually succumbed to the disease, is given below.

Path No. 26200—The patient, a colored female, age 40, was treated for enlargement of the thyroid with iodine, 12 years ago. Four and one-half years ago, she noticed a small lump in the upper outer quadrant of the left breast. This increased gradually to the size of a walnut. She struck it with a piece of wood after which it grew larger and became painful. The mass was excised elsewhere, in 1916, at which time it was 6 cm in diameter. There is no pathologic note on the specimen. One year later, in 1917, she noted a recurrence in the upper outer portion of the scar of the incision. This has gradually increased in size during the past three years and during the past two weeks it has become painful. Examination showed a normal thyroid gland. The left breast was enlarged and showed a scar 14 cm long at the site of the previous excision. In the midportion of the scar there were two masses, one, 9 cm in diameter internally to the scar and another 21.5 cm in diameter lateral to the scar. The overlying skin is attached to the masses and is slightly edematous. Both masses gave the sensation of fluid under tension on palpation, and over the larger mass there is an area 4 cm in diameter, which gives the impression of fluctuation. Two enlarged lymph nodes can be palpated in the left axilla. A radical operation was performed July 28, 1920. Both the masses showed hemorrhagic and grey, glistening, translucent material on section. In the larger tumor a small cyst was found. Pathologic examination showed definite gelatinous carcinoma. There are no metastases to nodes, the large axillary nodes showing tuberculous adenitis. The patient reported that she was well in 1924, was not heard from again. Her attending physician reports that she died of recurrent car-

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cinoma of the breast February 24, 1938, 18 years after the radical operation and 22 years after the first excision

Path No 17869—The patient, at the age of 36, in 1896, had her left breast removed for cancer. There is no note on the duration of symptoms or clinical findings prior to operation. The pectoralis minor was not removed and part of the axilla was not dissected. A pathologic note by Dr G P Briggs of New York, in 1896, states



FIG 20A, B and C—Path No 17869. Photograph of the patient, gross specimen and photomicrograph of a case of gelatinous carcinoma treated by mastectomy, in 1896. Dissection of the axilla and removal of the pectoral muscle with recurrent cancer was performed, in 1915. The patient died, in 1931, with mediastinal metastases, 35 years after the first operation.

that the tissue removed last February, consists chiefly of development of myxomatous tissue in the walls of the alveoli, the tumor removed is unquestionably a carcinoma which has undergone early degeneration into a mucoid substance of indefinite character. The degeneration has involved chiefly the carcinomatous cells, beginning in those nearest the alveolar wall and often leaving a central bunch of cells which are nearly normal.

Where breast tissue can still be recognized there is often seen proliferation of epithelial cells and infiltration of the fibrous stroma with small round cells. Tumors presenting extensive degeneration into homogeneous gelatinous material have usually been designated as colloid and I think this breast tumor is most properly called a "colloid carcinoma."

This letter of Dr Briggs, written in 1896, describes the tumor removed by Dr Bull.

Nine years later a mass appeared just below the axilla which gradually increased in size. In July, 1915, Dr Bloodgood operated upon the recurrent tumor and performed a partial excision of the mass in the apex of the axilla. He found it impossible to remove all the tumor because of its proximity of the larger nerves and vessels. Following this, the patient remained fairly well, but, in 1919, a mass appeared in the region of the clavicle. The patient received deep roentgenotherapy, in 1919, 1920, and in 1922. In 1926, an indurated mass developed, suggesting a recurrence beneath the clavicle. Further irradiation was given. In April, 1931, Dr Dandy performed an operation for the relief of pain because of symptoms of nerve pressure in the brachial plexus. At this operation tumor tissue, microscopically verified, was removed from the nerves. Pain, however, soon recurred with swelling of the arm and lymphedema.

In November, 1931, the arm was amputated. Erysipelas developed in the wound and the patient died, November 21, 1931, 35 years after the first operation with mediastinal metastases. At all the operations, subsequent to 1896, mucoid carcinoma could be demonstrated in the axilla or supraclavicular regions (Fig 20 A, B and C).

In diffuse gelatinous carcinoma with malignant epithelial cells of the scirrhous type, 10 cases had metastatic involvement of the lymph nodes. Only one of these patients was cured and this one remained well 14 years. Two died five years later of the disease and another had metastases to the opposite breast at the end of five years. One was dead four years later of other causes.

Six cases of gelatinous carcinoma with basal cells had metastases to the axillary lymph nodes. One died postoperatively, and another one year later of accidental death. Three died of the disease, 7, 18 and 35 years, respectively, after radical operation, and one was reported well 16 years later.

Twenty-four cases in the present series showed partial mucoid change. The predominant histologic picture, with few exceptions, was that of scirrhous carcinoma. The exceptional cases were comedo cancer (duct cancer) with areas of gelatinous carcinoma. Twenty of these cases have been adequately traced. Six survived the five-year period, and 14 are known to be dead of the disease. Eight of these cases showed skin involvement at the time of the first examination and 16 out of 24 had axillary involvement. On the other hand, in instances of gelatinous carcinoma with diffuse mucoid change, metastases occurred in 19 out of 57 cases, or approximately one-third. In the fatal cases the lungs were the most frequent site for internal metastases. Such involvement was reported in six cases. The liver, brain and skeleton were each involved twice.

CONCLUSIONS

Gelatinous carcinoma is a rare form of mammary cancer, and occurred 83 times in a series of 2,300 breast cancers. The peak of age incidence is between 46 and 50 years compared to 41 and 45 years for scirrhous cancer. The

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TABLE III

SYNOPSIS OF DATA RELEVANT TO 59 CASES OF GELATINOUS CARCINOMA

Path No	Age	Duration	Clinical	Operation		Result
60479	62-C	2 yrs	6 cm , near nipple, nipple bulges, skin involvement	C C *	5-22-35	Dead June, 1937
58398	55	3 mos	Multiple nodules, skin red	Excision	8- 7-37	
58216	34	21 mos		C C right	1-15-34	Well 4-21-38
				C C left	6-21-37	
57602	67	4 mos	4 cm L O Q , black and blue cyst	Excision	2- 3-37	
				C C	2- 5-37	
57290	41	4 mos	3 cm Clinically cyst gel flowed from wound	Excision	11-18-36	
				C C	11-20-36	
56134	46	1 yr	3 cm , central	C C	2-10-35	Well Sept 1937
55693	68	4 yrs	10 cm near nipple, 3 lumps felt, skin involvement	C C	9-25-33	Well 2-22-38
55022	69	6 mos	5 cm , U I Q , clinically cyst	Excision	3- 5-35	Well 3-28-38
52578	52	1 yr	3 cm U O Q , nipple protrudes	C C	1- 6-34	Dead 3-19-38
52081	76	2 wks	3 cm above nipple, second nodule above, nipple retracted	C C	9- 6-32	Dead 7-7-36, other causes
51228	50	6 mos	3 cm beneath nipple	C C right	5-15-33	Metastases left
				Excision left	1-10-38	axilla 2-24-38
50507	48	14 yrs	5 cm , skin discolored	Excision papilloma	1902	Well 2-27-38
				C C	1925	
				Excision	11-10-31	
				Excision	10-18-32	
49620	52	3 yrs	8 cm	Simple mastectomy	12- 6-32	Well 2-27-38
48052	40		4 cm near nipple	C C	5-10-32	Well 3-7-38
47241	45	3 mos	Near nipple	C C	4-15-30	Well 2-28-38
45703	44-C	Found routine	3 cm , U O Q	Excision	8- 5-29	Lost
				C C	8-10-29	
44868	41	2 mos	Central, nipple discharge	C C	5-10-31	Well 1-15-38
43462	66	3 days	2 cm , U I Q	Excision	Aug 1930	Well 2-22-38
				C C	Aug, 1930	
41940	34	9 mos	2 cm , central	Excision	7-23-29	Dead 4-26-35
				C C	7-24-29	
41018				Excision	10-29-30	
39396	57	3 mos	8 cm , L O Q , skin red	C C	4- 4-27	Well 2-26-38
39095	46		5 cm			
38598	79	48 yrs	5 cm , U I Q , nipple bulges	C C	12- 7-26	Dead 8-6-35, old age
37682	40	2 wks	6 cm , near nipple, lump in other breast	C C	5-24-23	Dead 9-15-28
36862	55	9 yrs	2 cm , clinically cyst	C C	7-16-25	
36257	36 C	6 yrs	Entire breast	C C	10-17-24	Dead 2-11-31
35465	44	2 yrs	0.5 cm , tumor previously removed opp breast U O Q	C C	5-13-24	Dead 2-17-25 other causes
35154	44		2 cm , upper breast	Excision	April 1924	Well 5-12-30
				X-ray therapy		
34353	66	8 yrs	2 cm central, bleeding and protrusion of nipple	C C	12- 8-23	Well 5-17-30
34033	48	3 yrs	6 cm , U O Q , clinically cyst	C C	10- 6-23	Well 3-14-38
32651	40	3 mos	2 cm , near nipple, breast cystic	C C	4- 6-23	Metastases 1937
30464	55	1 yr	6 cm central, skin discolored	C C	5-29-22	Dead 2-12-25
30448	60			C C	1920	Dead 1924, heart disease
29851			Autopsy specimen	Explored	1922	Dead Dec 1924 metastases to bone

*C C=Complete operation for cancer

SYNOPSIS OF DATA RELATIVE TO 59 CASES OF GLANDULAR CARCINOMA—*Continued*

Path No	Age	Duration	Clinical	Operation	Result
29697	32	2 yrs	2 cm, clinically cyst	Excision Mastectomy Excision axillary node	10-29-19 Feb 1922 Nov 1930 Well 4-6-38
27946	50			C C	1921 Well 3-30-35
27564	37	13 mos	Two lumps	C C	2-7-21 Dead 4-10-22 brain metastases
26200	40	6 yrs	10 cm	C C	6-3-20 Dead 2-24-36 recurrent cancer
25887	36	4 mos	Bleeding from nipple	C C	10-16-19 Dead 1921 metastases to lung
25249	30	5 mos		C C left C C right	10-29-19 11-2-20 Dead 1-29-21
24495	94		Autopsy specimen	None	
24433	70	2 yrs	8 cm U O Q	C C	4-28-19 Dead P O
24144	43	2 1/2 yrs	4 cm central clinically fibro adenoma	C C	2-27-19 Well 1930
21918	68	2 1/2 yrs	Bleeding from nipple	Mastectomy	7-26-17 Dead 1919 heart disease
18441	49	3 mos		Mastectomy	11-6-15 Well 1931
17869	36		Recurrence after 20 years	Mastectomy C C Irradiation	1896 7-22-15 1919-1922 Dead 11-21-31 cancer
17376	64	20 yrs	3 cm, discharge nipple, breast indurated	C C	4-17-15 Dead 1921
10011	43	6 yrs	4 cm U O Q, clinically fibro adenoma	C C	10-6-09 Lost
9260	58	2 mos	5 cm U I Q	C C	10-1-06 Dead 1909
8209	46	2 wks	2 cm U O Q	C C	5-16-07 Dead May 1912
7101	69	3 mos	5 cm above nipple	C C	2-22-06 Well Aug 1919
6821	40	1 mo	2 cm, U I Q, clinically cyst, bleeding from nipple	C C	11-10-05 Well 1924
5278	46	6 mos	5 cm O U Q skin involvement	C C	2-11-04 Dead 1905
4919	52		Central, bleeding from nipple	C C	6-23-99 Dead July 1902
4918	51		Beneath nipple	Mastectomy	6-7-02 Lost
4874	43	9 mos	5 cm, beneath nipple, bleeding from nipple	C C	6-4-03 Well 1930
4786	49	4 yrs	4 cm	Two previous excisions	1895-1899 Dead 1931 accident
				Excision	4-23-03
				Excision	6-6-06
4204	45	4 yrs	7 cm beneath nipple	C C	2-4-00 Dead 1-2-04
				Excision nodes neck	4-15-02
795	58	6 mos	3 cm I U Q, skin involvement	C C	3-2-95 Dead Nov 1904 pneumonia

discovery of a lump was the first sign noted by the patient in 80 per cent of the cases and in nearly half the cases the known duration of the mass prior to examination was a year or more, averaging 4.3 years. The average diameter of the tumor in the present series was 4.6 cm and only four tumors were 10 cm or over in diameter. The most prevalent sites in the breast are the outer upper quadrant and central zone.

There are four chief findings on clinical examination which suggest a

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diagnosis of gelatinous carcinoma The first, is the relatively small size of the tumor in comparison with the long duration of symptoms The second, is the protrusion and enlargement of the nipple on the affected side The third, is the cystic character of the growth on palpation, the growth being differentiated from a benign cyst by aspiration of characteristic mucoid material The fourth, is the presence of a "swish" on firm pressure, as originally described by Halsted

TABLE IV

SYNOPSIS OF DATA RELEVANT TO 24 CASES OF SCIRRHUS CANCER WITH MUCOID CHANGE

Path No	Age	Duration	Clinical	Operation	Result
48446				C C	7- 4-32 Dead 3-15-33, metastases
45703	44-C	Routine examination	3 cm , upper outer quadrant	Excision C C	8- 5-29 Lost
41029	28	1 yr		C C	3-26-27 Dead 7-26-28 heart disease
41018				Excision	10-29-30 Lost
40882	48	4 yrs	0.5 cm , recurrent	C C	10- 9-28 Dead 1930 metastases to spine
39347	73		5 cm , cystic	Excision	5-29-26 Well 1932
39146	68	18 mos	Discharge nipple ulceration	C C	3-16-27 Dead Sept 1933, phlebitis
39112	47	18 mos	Large tumor	C C	4-14-27 Dead 1928, metastases to lungs
38540	34	3 wks	3 cm nipple zone	Excision C C	11-12-26 Dead 11-23-27 metastases to brain
37406	40	4 mos	Diffuse, two tumors	C C	11-18-26 Dead June 1934, cancer
32416		1 yr	5 cm , nipple freely movable	C C	12-26-25 Dead 1926, metastases to lung
31853			Cystic	Excision	11-28-22 Dead
26068	32	2 wks		C C	5- 2-20 Dead 2-7-24, carcinoma stomach
23633	54	11 mos	6 cm , near nipple	Excision C C	12- 6-15 Well 3-4-38
18592	78	6 mos			8-27-18 Dead 1919 metastases
16076	39	2 yrs	1 cm , skin changes, breast infiltrated	C C	7-24-14 Dead 8-6-15, metastases to lung
15549	43	2 days		C C	4- 1-17 Well 2-23-25
10630	48	5 yrs	14 cm upper hemisphere	C C	6- 6-10 Lost 1927
9733	32	2 yrs	8 cm , nipple zone, pig-skin	C C	6- 4-09 Dead 1911
9077	37	3 mos	Outer lower quadrant, skin nodules	C C	7- 2-08 Dead 1914
8467	46	9 mos		C C	9-16-07 Dead 1909
8039	31	8 mos		C C	3-21-07 Dead 1908
7567	49	3 yrs	9 cm , nipple zone, nodes palpable	C C	9-21-06 Lost
5078	45	2 mos	10 cm , skin metastases, nodes palpable	C C	1904 Dead 3 mos later

Mucoid cancers on gross and microscopic examination may be diffusely or partially gelatinous The gelatinous material has a characteristic gray, translucent appearance, resembling tapioca Microscopically, mammary can-

cancers with diffuse gelatinous change originate in papillary cancer, adenocystic basal cell cancer, or slowly growing adenocarcinoma. The mucoid material is secreted by the epithelial cells of the tumor. Cancers showing partial mucoid change are usually of the scirrhous type. In the present series, 59 of 83 cases showed diffuse or typical gelatinous change. Thirty-four of 45 of these patients, who were adequately traced, survived the five-year period—75 per cent of five-year cures. Six of these patients eventually died of recurrent disease, one case 16 years, another 18 years after radical mastectomy.

Twenty of 24 cases with carcinomata showing partial mucoid change were adequately traced. Only five survived the five-year period—30 per cent of five-year cures. In the present series, the five-year survivals for all types of mammary carcinomata showing mucoid change (diffuse or partial) was 60 per cent.

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THE DIFFERENTIAL DIAGNOSIS OF HYPERPARATHYROIDISM*

WITH SPECIAL REFERENCE TO POLYOSTOTIC FIBROUS DYSPLASIA

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IN THE 12 years that have passed since Mandl, at the suggestion of Erdheim, first removed a parathyroid adenoma in a case of hyperparathyroidism, the number of reported cases of this disease has increased considerably. Up until February, 1936, Wilder and Howell were able to collect 135 cases, which, upon careful analysis, were unquestionably authentic instances of the disease. Undoubtedly, there have been many others which have not been reported.

The clinical, roentgenographic, and chemical aspects of hyperparathyroidism have been stressed so frequently in the past decade that the disease has become familiar to the medical profession at large.

It may be well, however, to again state that the various manifestations of hyperparathyroidism are dependent upon the secretory hyperactivity of one or more parathyroid adenomata which bring about a profound disturbance of calcium and phosphorus metabolism, and that surgical removal of the tumor results in either complete cure or marked amelioration of the symptoms. The disease, which occurs more frequently in females and usually in middle life, is measured, as a rule, in terms of years. It is characterized by bone and joint pain, muscle weakness, localized bone swellings, pathologic fractures, particularly of the extremities and ribs, disturbances of gait, and, in advanced cases, deformities of the bones. There may be other symptoms which become so prominent as to cloud the more important aspects of the clinical picture. These are attacks of intractable nausea and vomiting, polyuria and polydipsia, renal colic, anorexia, severe constipation, loss of weight, and secondary anemia.

The explanation of the roentgenologic findings rests upon a knowledge of the disturbance of physiologic activity of the parathyroid tumor. Normally, it is the function of the parathyroid bodies to control calcium and phosphorus metabolism within the narrow confines of fairly constant blood serum values of 9.5 to 10.5 mg. of calcium per 100 cc. and 3 to 3.5 mg. of phosphorus per 100 cc. When parathyroid activity is increased, because of the presence of a hyperfunctioning tumor, the serum calcium level is increased and the phosphorus decreased due to the fact that greater quantities of calcium salts are withdrawn from the bones. Usually, increased phosphatase activity can be demonstrated. The effect of prolonged withdrawal of calcium salts from the skeleton becomes evident upon roentgenologic examination. The bones of the

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skull present a finely granular appearance. The long bones appear porotic with thinning of the cortex and trabeculae. There may be cyst formation in the center of the shaft. The pelvic bones are frequently cystic. The vertebrae present a coarsely granular pattern similar to that seen in the skull. Due to softening of the skeleton, deformities result from gradual collapse of supporting structures such as the spine, pelvis and thoracic cage.

Up to the present time, most observers have agreed that a diagnosis of hyperparathyroidism should be made when, in addition to the clinical symp-



FIG. 1.—Case 1. Roentgenogram of skull showing a finely granular appearance of the bones of the calvarium due to absorption of calcium.

toms and roentgenologic findings already enumerated, there is found a hypercalcemia, a hypophosphatemia, an increase in the serum phosphatase and a proven negative calcium balance. In fact, the combination of these laboratory findings is considered pathognomonic of the disease. However, the course of events and the laboratory findings in Case 3, herewith appended, tend to cast considerable doubt as to the validity of considering these laboratory tests as pathognomonic of hyperparathyroidism. As a result of this experience it may become necessary to reconsider the entire problem in order to establish criteria which would aid in the increasingly difficult aspects of differential diagnosis.

In order to emphasize some of the points to be considered in differential diagnosis, two cases of proven hyperparathyroidism are briefly reported.

Case 1—M. L., female, age 29, single, referred by Dr. Reuben Ottenberg on March 30, 1937. About 18 months previously, she had consulted her dentist concerning the re-

removal of a tooth. Roentgenologic examination of the jaw at the time showed bony rarefaction involving the maxilla and mandible. A few months later, after a comparatively slight injury, the patient fractured the left patella, which, however, united without much difficulty. About one year ago, roentgenologic examination of the long bones demonstrated small cystic areas in the lower ends of the right radius and ulna. At that time the blood calcium was reported to be 14 mg per 100 cc, and the phosphorus 2 mg.

A roentgenologic examination of the entire skeleton showed (a) Marked decalcification of the skull, which presented a sieve-like appearance, (b) the radius and ulna were decalcified, with small cystic areas in the proximal end of the left radius and distal ends of right radius and ulna, (c) the knees showed marked bony absorption in the femora, with cysts in the left patella, (d) the pelvis showed cystic bone absorption in the right ilium and a suspicious area in the left sacrum. Roentgenologic examination of the kidneys showed no calculi (Figs 1, 2 and 3).

Physical examination was negative. Urine and blood examinations showed no abnormalities. Just previous to admission to the hospital, the serum calcium was 11.8 mg, phosphorus 2.4 mg and phosphatase 30.5 Bodansky units.

The patient was admitted to the Mt Sinai Hospital April 7, 1937. Calcium balance studies showed that, after a three-day diet containing 300 mg of calcium, the excre-



FIG 2—Case 1. Roentgenogram of left knee showing cyst in left patella and coarse trabeculation of the femur and tibia.



FIG 3—Case 1. Roentgenogram of pelvis showing cystic disease involving the ilium.

tion of calcium was 1 073 mg, 771 mg appearing in the urine and the remainder in the feces. In other words, there was a negative calcium balance of 773 mg.

Operation—April 13, 1937. A parathyroid adenoma measuring 4.5 by 2 by 1 cm was found at the lower pole of the right lobe of the thyroid gland (Fig 4). It dipped downward, behind the sternum, toward the mediastinum. Both sides of the neck were explored, but no other tumors were found. Two normal parathyroid bodies were found on the left side.

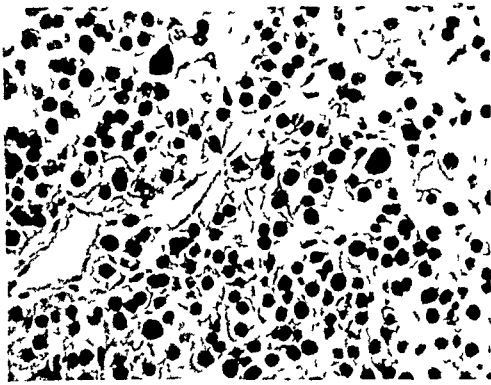


FIG 4.—Case 1. Photograph of tumor of the parathyroid removed at operation. Microscopic section of it which shows that the tumor was composed mainly of chief cells.

Pathologic Examination of the tumor showed it to be quite cellular. It was composed mainly of pale, water-clear chief cells, with frequent giant cells, and some small groups of oxyphilic cells (Fig 4).

Convalescence was uneventful until the fourth day, when she developed headache, tingling in the face, hands and feet, and diarrhea. There was a positive Chvostek's sign. At this time the serum calcium was 6.9 mg and the phosphorus 3 mg. This mild tetany responded promptly to parathormone and calcium gluconate. At the time she left the hospital, April 23, 1937, the serum calcium was 9 mg.

Since her discharge the patient has improved steadily. There has been no recurrence of symptoms and the blood figures are normal. The patient has returned to work.

Case 2—Hosp No 407735. An Italian woman, age 36, was admitted to the Medical Service of the Mt Sinai Hospital September 8, 1936. For the preceding year she had been receiving treatment in the Out-Patient Department for a right renal calculus. She complained of recurring attacks of pain in the right

lumbar region, which had begun four years previously, following a pregnancy. The pain occasionally radiated to the right groin. It was never accompanied by chills, fever or hematuria. The past history was irrelevant.

Physical examination was negative. The blood count was normal, as was also the urinalysis. Blood sugar, 90 mg; urea nitrogen, 15 mg; serum calcium, 13 mg; serum phosphorus, 4 mg. Phosphatase determination showed eight King-Armstrong units. A later blood examination showed the calcium to be 11.8 mg and the phosphorus 3.5 mg. Roentgenologic examination of the skull and long bones failed to reveal any abnormality. A suspicious rarefied cystic-like area was seen in the left ilium. The patient was discharged September 30, 1936, as a possible case of hyperparathyroidism.

She was readmitted April 26, 1937, complaining that she had been having generalized bone pains for the preceding three months. These were boring in character and involved mainly the left shoulder, knees and hips. She also experienced occasional attacks of nausea without vomiting.

Physical examination was again negative. The roentgenologic examination was repeated and disclosed an enlargement of the previously noted cystic area in the left ilium as well as the presence of two small calculi in the right kidney pelvis (Fig 5). Serum calcium, 11.6 mg; phosphorus, 3.4 mg; calcium balance studies revealed a daily negative balance of one gram.

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FIG 5—Case 2 Roentgenogram of pelvis showing cystic rarefaction in the left ilium

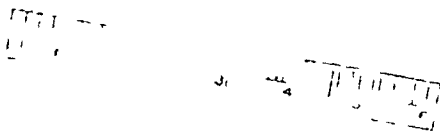


FIG 6—Case 2 Photograph of tumor of a parathyroid removed at operation. This represents about two thirds of the original size of the tumor. Microscopic section of it shows that the tumor was composed mainly of chief cells



FIG 7—Case 3 Roentgenogram of the left hip showing an incomplete fracture of the neck of the femur and the apparent cystic rarefaction of the neck and shaft of the femur



FIG 8—Case 3 Roentgenogram of the skull showing the finely granular appearance similar to that seen in Fig 1. In addition, there is apparent cystic rarefaction of the occipital protuberance

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Operation—April 30, 1937 Considerable difficulty was encountered in locating the parathyroid adenoma, which was finally found embedded in the substance of the right lobe of the thyroid near its postero-external surface The adenoma which measured 3 by 2.5 by 1.5 cm, presented the typical reddish-brown color It was removed *in toto* Search was made for additional tumors, but none were found Two normal parathyroid bodies were demonstrated Histologic examination of the adenoma showed it to be composed mainly of chief cells (Fig. 6)

Convalescence was uneventful other than for the development of a positive Chvostek's sign which persisted for one week The serum calcium figures were 8.7, 9.7 and 9.1 mg The patient was discharged May 15 in excellent condition

When last seen, November 8, 1937, she stated that she no longer had any bone pains and that the pain in the right lumbar region had also disappeared



FIG. 9—Case 3. Roentgenogram of the right humerus which presents an appearance similar to that seen in osteitis fibrosa cystica. Closer examination indicates thinning of the cortex which, on microscopic section, is found to be due to erosion from the endosteal surface. The apparent cystic areas represent fibrous tissue containing islands of immature bone.

In contradistinction to the above cases, I wish to report, in detail, the history of the patient which forms the basis of this paper.

Case 3—M. S., male, age 47, was seen May 2, 1937 in Richmond, Va., in consultation with Drs. Wm. H. Higgins, Carrington Williams, Bigger and Alice Bernheim. Approximately two months previously, while in England, the patient had developed pain and lameness in the left hip. Three weeks later while playing ping-pong on board ship, he experienced a sudden, sharp pain in the left hip. He was able, however, to carry on his activities, but with some difficulty. Roentgenologic examination demonstrated an incomplete fracture of the neck of the left femur without displacement or impaction (Fig. 7). In addition, there was found an extensive rarefaction of the neck and shaft of the femur.

which suggested to Doctor Higgins the possibility of osteitis fibrosa cystica. He was admitted to St. Luke's Hospital, Richmond, for study.

Roentgenologic examination of the remainder of the skeleton disclosed what appeared to be cystic rarefactions in the lower end of the left femur, lower end of right humerus, occipital bone, pelvis and two ribs (Figs 8, 9 and 10). Blood serum examination showed calcium, 13 mg, and phosphorus, 2.8 mg per 100 cc.

On the natural assumption that the patient was suffering from hyperparathyroidism resulting in a pathologic fracture of the left hip, exploration of the neck was undertaken by Dr. Carrington Williams. After a prolonged and thorough search, no parathyroid adenoma was demonstrable. Convalescence was uneventful and the wound healed by first intention.



FIG 10—Case 3. Roentgenogram of left femur. The findings here are similar to those seen in Fig. 9. They may be easily mistaken for the roentgenologic evidence one sees in cases of osteitis fibrosa cystica.

Careful inquiry into the patient's past history brought out the interesting fact that since childhood the left leg had been one inch longer than the right, and that for the past ten years the patient had had frequent pains in the left thigh and knee.

The patient was transferred to New York in order that careful calcium balance studies might be undertaken in the hope of definitely establishing a positive diagnosis, and entered the New York Hospital May 4, 1937.

Examination was negative except for a prominent occipital protuberance and the fact that the left lower extremity was 3 cm. longer than the right.

Laboratory Data—Urine, negative, there was no Bence-Jones protein, hemoglobin, 94 per cent, red blood cells, 4,570,000, white blood cells, 8,600, polymorphonuclear leukocytes, 66 per cent, lymphocytes, 19 per cent, monocytes, 11 per cent, basophiles, 4 per cent, serum calcium, 11.3 mg, phosphorus, 3.2 mg, and phosphatase, four Bodansky units.

The patient was placed on a three-day diet containing 300 mg of calcium. During this time, bowel function was normal. The diet was continued for three more days and all urine and feces excreted during this second period were examined for calcium excretion. The measured calcium intake during the initial three-day period obviates the possibility of error from additional calcium which may be present in the intestinal tract. Examination of the stool and urine specimens collected during the second period showed an excretion of 1547 mg of calcium, 841 mg appearing in the urine and 706 mg in the feces. In other words, the patient presented a marked negative calcium balance. This seemed fairly conclusive confirmatory evidence of the existence of hyperparathyroidism.

Before undertaking a second neck exploration, I asked Dr. H. Jaffee to see the patient. After a prolonged examination of the roentgenograms and the laboratory data, he formed the opinion that the evidence was overwhelmingly in favor of a diagnosis of hyperparathyroidism, but reserved a 5 per cent possibility that the patient might be suffer-



FIG. 11.—Case 3. Microscopic section of the bone biopsy taken from the left femur which shows fibrous tissue metaplasia of the bone marrow containing scattered islands of immature bone. This is one of the characteristic findings of "polyostotic fibrous dysplasia."

ing from polyostotic fibrous dysplasia. He concurred in the opinion that the neck should be explored again.

Operation—May 14, 1937. The technical difficulties were considerable because of extensive scarring. A thorough exploration of the neck and superior mediastinum was made, but no parathyroid adenoma was found. The wound was closed. Through a longitudinal incision on the lateral aspect of the left thigh, the upper part of the femur was exposed and a liberal section of cortex and subjacent tissue was removed. The cortex was found to be extensively eburnated and somewhat thinned. The marrow was replaced by dense fibrous tissue which had a rubbery consistency.

Pathologic Examination of the bone biopsy material by Doctor Jaffe showed replacement of the normal marrow by vascular fibrous tissue which contained numerous trabeculae of immature bone (Fig. 11). There were no giant cells and no evidences of active resorption or transformation of the metaplastic new bone. *Diagnosis*—Polyostotic fibrous dysplasia.

Convalescence was uneventful. The operative wound healed without incident and the patient returned to Richmond the end of May. Repeated roentgenologic examinations of the hip showed subsequent solid union at the site of fracture. At Doctor Bernheim's sug-

gestion the patient was placed on a high calcium and high vitamin diet which he has continued to date. He was advised to avoid undue physical activity in order to guard against possible fracture. He has resumed his business activity and now feels well. A recent check-up roentgenologic examination of the skeleton indicates that some calcification of the involved bones is taking place. The serum calcium is 8.7 mg, phosphorus, 3.4 mg, phosphatase, 5.9 Bodansky units.

DISCUSSION—There will appear in the Archives of Surgery, vol. 36, 874-898, May, 1938, an article by L. Lichtenstein on "Polyostotic Fibrous Dysplasia." The material forming the basis of this paper was assembled in the laboratory of Dr. H. Jaffe at the Hospital for Joint Diseases in New York. The following discussion of the disease is based upon conversations with Drs. Jaffe and Lichtenstein, to whom appreciation is hereby expressed for the privilege of reporting, briefly, the results of their investigations.

The disease, which Lichtenstein gives the name "Polyostotic Fibrous Dysplasia," has been, heretofore, reported in the literature under a great variety of titles, such as "Osteo-Dystrophia Fibrosa Unilateralis," "Unilateral Recklinghausen's Disease," "Unilateral Polyostotic Osteitis Fibrosa," "Focal Osteitis Fibrosa," "Osteitis Fibrosa in Multiple Foci," "Osteitis Fibrosa with Formation of Hyaline Cartilage," "Osteitis Fibrosa Disseminata," etc. Lichtenstein and Jaffe have, up to the present time, seen nine instances of the disease, four in their own hospital and five at other institutions, including the case reported in this paper.

A review of the case histories would seem to indicate that the age of onset of symptoms is in childhood or early adolescence, and that females are predominantly affected. The common presenting symptoms are limp, bone pain, deformity of the affected limb and pathologic fracture. It may take years for the disease to progress to a point where medical aid is sought. Our patient was age 47 before severe symptoms developed, although bone pain had been present for the preceding 10 or 12 years.

A peculiar feature is the tendency of the bone lesions to be predominantly unilateral in distribution, either side being affected without preference. Exceptions to this, however, are not uncommon, as is indicated in our own case. Although the femur and tibia are most frequently involved, it is not unusual to find evidences of the disease in the radius and humerus as well. The skull and pelvis may also be affected.

The characteristic findings on roentgenologic examination may be summarized as follows: (1) Broadening or expansion of the bone, (2) thinning of the cortex, (3) characteristic rarefied and apparently trabeculated appearance, (4) secondary deformities of the affected bones. Pathologic fracture of the neck of the femur is common. Inasmuch as the condition is frequently erroneously interpreted as osteitis fibrosa cystica, or Recklinghausen's disease, it is important to examine the entire skeleton roentgenologically in order to determine whether the bone lesions are unilateral in distribution. This is an important point in differential diagnosis. As will be pointed out, the bones involved in polyostotic fibrous dysplasia do not contain cysts, in contradistinction-

tion to hyperparathyroidism, and this must be borne in mind when interpreting the roentgenograms

The basis of Lichtenstein's interpretation of the pathologic features of the disease is adequate biopsy material obtained from nine cases. The bone cortex is considerably thinned out, due in part to resorption, but largely to erosion of the endosteal surface by the proliferating fibrous tissue replacing the marrow cavity. There is no evidence of periosteal proliferation or new bone deposition. The medullary cavity is filled with fibrous tissue which is grayish-white in color and has a peculiar consistency described as spongy or rubbery. It has also been noted to be gritty. This fibrous tissue is composed of spindle cells with oval, pale staining nuclei. In some areas the basic connective tissue has undergone a fibroblastic differentiation into mature connective tissue containing a large amount of collagen. Dispersed irregularly in this fibrous tissue may be seen small trabeculae of primitive, poorly calcified new bone. The fibrous tissue appears relatively avascular. There may be seen small nests of giant cells, resembling osteoclasts. Occasional islands of hyaline cartilage may be found within the fibrous tissue. This is not a constant finding.

I wish to quote verbatim from Lichtenstein's paper in order to express his views on the pathogenesis of this disease. "The characteristic pathologic feature of polyostotic fibrous dysplasia appears to be a disturbed function or development of the bone-forming mesenchyme, which results in replacement of the spongiosa and filling of the medullary cavity of affected bones by fibrous tissue in which trabeculae of poorly calcified primitive new bone are developed by osseous metaplasia. The seemingly complex histologic picture becomes much easier to interpret if one predicates the multipotential capacity of this undifferentiated fibrous tissue. The latter normally gives rise to the spongiosa and to the myeloid or fatty marrow, but under pathologic conditions it may develop in several anomalous ways. By osseous metaplasia, it gives rise to osteoid and primitive fiber bone. By cartilaginous metaplasia, it gives rise to sporadic, isolated islands of hyaline cartilage, which tend to become calcified. By fibroblastic differentiation, it gives rise to mature collagenous connective tissue. Finally, by coalescence of its nuclei, it may give rise to multinuclear cells, indistinguishable from osteoclasts. Whatever stimulates the continued perverted activity of the undifferentiated fibrous bone-forming mesenchyme, or initiates the disorder remains a matter of conjecture. The clinical history of symptoms dating back to early childhood strongly suggests a congenital basis for this curious anomaly."

In Lichtenstein's series, serum calcium determinations ranged between 9.8 and 11 mg per 100 cc. The serum phosphorus estimations showed no significant change. In three of his cases, the phosphatase was considerably increased, namely, 17, 18 and 22 Bodansky units. Lichtenstein feels that the increased phosphatase values in polyostotic fibrous dysplasia afford additional evidence to support the contention of Bodansky and Jaffe that the activity of the enzyme phosphatase is proportional to the stimulus to new bone

formation. It is interesting to note that the serum values of the patient reported in this paper were such as to confuse the diagnostic problem considerably. In Richmond, the serum calcium was 13 mg and the phosphorus 2.8 mg. When these were repeated in Beinheim's laboratory at the New York Hospital, they were 11.3 mg of calcium and 3.2 mg of phosphorus. The phosphatase determination was four units.

In none of the cases studied at the Hospital for Joint Diseases were calcium balance studies made. In our own case, such studies showed an excretion of 1547 mg of calcium in the urine and feces over a three-day period, during which a measured diet containing 300 mg was ingested. This indicated a



FIG. 12.—Microscopic section from a typical case of "polyostotic fibrous dysplasia" showing the fibrous tissue filling the medullary cavity and thinning of the bone cortex due largely to erosion of the endosteal surface. Dispersed irregularly in the fibrous tissue are small trabeculae of primitive poorly calcified new bone. (From the collection of Dr. Henry Jaffe, Hospital for Joint Disease, New York.)

marked negative calcium balance which, in conjunction with all other findings, was considered conclusive evidence of an existing hyperparathyroidism.

The importance of the laboratory and roentgenologic findings in Case 3 now becomes obvious. It is evident that a patient with polyostotic fibrous dysplasia may present all the clinical and confirmatory laboratory evidence usually associated with hyperparathyroidism, or osteitis fibrosa cystica.

CONCLUSIONS

It is suggested, therefore, that the surgeon, when confronted with suspicious bone lesions evident in the roentgenograms, and serum estimations of calcium and phosphorus which are outside the normal limits, and in spite of the fact that calcium metabolism studies may show a negative balance, should not be too hasty to advise exploration of the neck for a parathyroid adenoma. It is suggested further that, when doubt exists as to the diagnosis, additional

investigation should be undertaken to clarify the situation. This consists, first, of roentgenologic examination of the skeleton to determine whether the bone lesions have a predominantly unilateral distribution and second, the performance of a bone biopsy. The latter will definitely establish the diagnosis by differentiating the characteristic histologic pictures of polyostotic fibrous dysplasia and hyperparathyroidism (Figs 12 and 13).



FIG 13—Photomicrograph from a typical case of osteitis fibrosa cystica which should be compared with Fig 12. This indicates that most of the bone change has taken place in the cortex with cystic degeneration and bone absorption as the predominant features. There is little or no change in the medullary cavity. (From the collection of Dr Henry Jaffe, Hospital for Joint Disease, New York.)

DISCUSSION—DR EMIL GOETSCH (Brooklyn) said that Doctor Garlock had drawn attention to some very interesting as well as anomalous conditions which simulate parathyroid dysfunction but which are not due to parathyroid hyperactivity. The present status of knowledge concerning the parathyroid is rather confused but, as with previous clinical syndromes, the time will come when those due to parathyroid dysfunction will be more clearly differentiated.

The first two cases were unusually illustrative of the clinical conditions typical of parathyroid adenomatous tumors. There were the usual blood changes with elevation of the calcium level and a diminution in the phosphorus content. There was an increase in the phosphatase and the bone changes first described by von Recklinghausen were typical of those found in instances of hyperactivity of the parathyroid. It is very satisfactory to have found parathyroid adenomata with the establishment of the real cause of the disease, and it is very satisfactory to have obtained such good results after the removal of the parathyroid tumors. Incidentally, too, the calcium and phosphorus content of the blood returned to normal, and there was an improvement in the condition of the bones due to redeposition of calcium in those areas from which calcium had been absorbed.

The third case was rather troublesome in that the bone changes were certainly suggestive of those found in hyperparathyroidism and there was associated a negative calcium balance, an association of findings very suggestive of parathyroid tumor. After most careful search, no parathyroid tumor or adenoma was found. Doctor Garlock called attention to the disease designated as "polyostotic fibrous dysplasia" which exhibits the findings just described and warned against being too hasty in operating for a supposed instance of

parathyroid tumor even in the presence of a negative calcium balance and rarefaction of the bones

The last case further demonstrated the great value of calcium balance studies and that one cannot rely upon blood calcium findings alone. Calcium balance determinations over the three-day period are far more valuable than a few isolated blood calcium determinations. Thus, a high calcium change may be present due to failure of excretion or, on the other hand, a relatively low calcium may be present in instances of rapid excretion. The value of calcium balance determination, therefore, is obvious. Doctor Garlock warned against too prompt exploration of the neck before a very careful clinical investigation has been made. Too many conditions in which calcium deposits have been found, such as arthritic changes or arteriosclerosis, have been attributed to parathyroid dysfunction. Even scleroderma or arteriosclerosis has been attributed to disturbances of parathyroid function. In a recent case of this kind with extensive sclerosis, stiffness of the face and "wooden" fingers, Doctor Goetsch was prevailed upon to explore for parathyroid tumor but after most careful search nothing was found, although there was present an interesting generalized fibrous sclerosis, deep as well as superficial. Incidentally a small isolated tumor of thymus tissue was found at the right lower pole. At times it is difficult to identify, absolutely, parathyroid tissue for it may be atypical and thus be confused with the appearances commonly noted in true lymph nodes or hemolymph nodes commonly found in the region of the parathyroids. Also there may be an admixture of lymphoid tissue. Illustrations are sometimes exhibited which appear more like lymphoid tissue than true parathyroid tissue.

DR HENRY L. JAFFE (New York) thanked Doctor Garlock for his generous acknowledgment of the work of Doctor Lichtenstein and himself in connection with "polyostotic fibrous dysplasia," the pathology of which they had been able to clarify on the basis of cases coming under their observation which helped to establish it as an entity.

A number of points bear reemphasis. One rarely observes a clear-cut increase in the serum calcium value in "polyostotic fibrous dysplasia." Of the cases observed by Doctor Jaffe only two had figures above 11, and those figures were below 11.5 mg per 100 cc. The serum phosphorus figures (which are also important in the diagnosis of true cases of hyperparathyroidism) were more or less normal in all the cases observed. The serum phosphatase activity values were high except in one case, and that was a man of 47. His biopsy specimen showed relatively little new bone in the fibrous tissue filling the marrow cavity and, furthermore, there was not very extensive involvement in his case. In younger subjects, with more extensive lesions, the phosphatase values were high and, indeed, as high as in hyperparathyroidism.

The marked negative calcium balance reported by Doctor Garlock threw Doctor Jaffe off altogether. On empiric grounds he could not believe that cases of "polyostotic fibrous dysplasia" should show pronounced negative calcium balances. In fact, he considered making calcium balance studies on several of his cases, but since the osseous involvement was not generalized and was often quite limited, he felt certain that the calcium balance studies would show nothing remarkable. It is true that Doctor Goetsch emphasized the value of calcium balance studies and many people have been stressing their value in diagnosis of various skeletal diseases. Nevertheless, Doctor Jaffe doubted the value of the information obtainable from a three-day calcium balance study as done by present methods. The fact is that a normal person on a diet containing 100 mg of calcium shows in a three-days' balance study a negative calcium balance and the calcium balance studies only measure the degree of negativeness from person to person. Doctor Jaffe did not doubt Doctor Bernheim's figures for Doctor Garlock's case, yet he was skeptical.

that subjects with "polyostotic fibrous dysplasia" show pronounced negative balances. He emphasized that it is of the utmost importance to clarify this point in the differential diagnosis between this condition and hyperparathyroidism. Certainly if studies of additional cases show that the calcium balance is severely negative, then there is another confusing point in the differential diagnosis between it and hyperparathyroidism. Doctor Jaffe hoped for the sake of diagnosis that it would prove to be otherwise.

Regarding roentgenologic findings, Doctor Jaffe affirmed Doctor Garlock's statement that there is a tendency for the lesions to be unilateral. Furthermore, the lesions, statistically, tend to concentrate in the femur and tibia, although he had seen them in the calvarium and particularly in the occipital bone, also in the ribs, in the vertebrae, in the pelvic bones, and even in the small bones of hands and feet. The reason why cases of "polyostotic fibrous dysplasia" are misdiagnosed as hyperparathyroidism is that the fibrous tissue growing in the marrow cavity erodes the inner surface of the cortex and may even distend the bone, and, of course, the bone shadow is suggestive of a cyst. Actually these bones are not cystic. When one penetrates the cortex, one finds the marrow cavity filled by a hard and almost rubbery tissue. Even where the picture is, roentgenographically, clearly that of a cyst, this type of tissue exists.

One important point in the roentgenologic differential diagnosis between "polyostotic fibrous dysplasia" and hyperparathyroidism is rarefaction of the cortex of most bones in the latter and the absence of cortical rarefaction except in the affected bone in the former.

DR CARL G. BURDICK (New York) asked Doctor Jaffe regarding the outcome of some of the cases he had followed.

DOCTOR JAFFE answered that the first case he saw was a girl who at the time of his first observation (1926) showed involvement of a number of ribs, one femur, and one tibia. She had a fracture through the neck of the femur. She left the Hospital for Joint Diseases and some years later Doctor Jaffe traced her to Long Island College Hospital where a bone graft had been inserted in the femur. She became a mother of two children and her illness was not particularly aggravated by the pregnancies. She still has the disease and presumably she will go on having it. Some of the lesions may subside somewhat as she becomes older. The fibrous tissue may become more collagenous and the condition consequently less progressive.

DR BRADLEY L. COLEY (New York) recalled a case of malignant tumor of the parathyroid gland which he showed before the New York Surgical Society in 1936. At that time it was assumed that the changes in the patient's spine, which originally brought him under Doctor Coley's care, were due to hyperparathyroidism associated with the tumor. The subsequent course, however, proved that the lesion in the spine was really a metastasis, and when last seen the patient was growing rapidly worse. In retrospect, the case represents one of malignant tumor of the parathyroid (adenocarcinoma of parathyroid origin) with metastasis to the lumbar spine.

DR JOHN H. GARLOCK (New York), in conclusion, said that Doctor Jaffe's remarks about calcium balance studies were very well taken. Nevertheless, he could not alter his belief in Doctor Bernheim's figures. Doctor Bernheim has done many calcium balance studies over a long period of time in her own laboratory in New York Hospital, and also has a technician who has been working under her for many years, and knows how to carry out the studies. In the case presented these studies definitely showed a marked negative calcium which Doctor Garlock considered to be a very important finding.

THE TREATMENT OF POSTOPERATIVE TETANY WITH DIHYDROTACHYSTEROL*

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THE parathyroids were first recognized as independent organs by Sandström in 1880,¹ but Gley² (1892) was the first to show that their removal was associated with the production of tetany. Two outstanding facts have long been known regarding the physiology of the parathyroids as glands of internal secretion: (1) Their influence on calcium metabolism and (2) the specific relation of hypoparathyroidism to altered irritability of the nervous system, these two relationships being closely associated.

Excision of the parathyroid glands of dogs produces, after a latent period of variable length, an acute tetany, which is characterized by a hypocalcemia. The symptoms may be directly controlled to a greater or less degree by means of (a) injections of extracts of the parathyroid glands (Beche,^{3, 4} and Berkeley and Beebe⁵), (b) by dietary control in conjunction with the administration of calcium^{6, 7}, (c) symptomatically by means of narcotics and hypnotics.⁸ The effectiveness of such therapy suggested that the function of these glands was the regulation of calcium metabolism, i.e., that they control the absorption and retention of calcium as shown by MacCallum and Voegtlin.⁹ However, other metabolic changes, which might favor the development of convulsions following parathyroidectomy, likewise occur. These changes, including depressed liver function (Carlson and Jacobson^{10, 11}), the appearance of guanidine, histamine and similar toxic bases in the urine (Koch^{12, 13}), diminished carbohydrate tolerance (Underhill and Saiki¹⁴), are probably of secondary concern.

The basic importance of the physiology of the parathyroid glands is due to their interrelationships with other glandular structures, the fundamental relation of calcium metabolism to cellular permeability and function, and from a clinical standpoint to their relation to idiopathic and postoperative tetany. The latter condition develops to a greater or lesser degree following either (a) the accidental removal of one or more of these structures during the course of a thyroid operation, or (b) their destruction through interference with their blood supply, postoperative infection, or scar tissue compression. Under such conditions, postoperative tetany is characterized by a hypocalcemia of greater or lesser degree. The severity of the symptoms parallels as a rule the degree of hypocalcemia, but rather wide individual variations are to be noted in different patients. However, restoration of normal values for a particular patient results in a complete disappearance of symptoms of tetany.

* Read before the New York Surgical Society, New York, N. Y., April 28, 1937.
Submitted for publication June 19, 1937.

during the period in which a normal calcium balance is maintained or certain minimum blood calcium values are exceeded

The normal blood calcium and phosphorus values vary from 9 to 11 mg and from 3.2 to 4.5 mg per 100 cc of blood serum, respectively. As a rule, symptoms of tetany become manifest when the serum calcium values fall to, or below, 7 mg, while the serum phosphorus values on the other hand usually rise. It is quite impossible, however, to establish an arbitrary tetany level for calcium values. Symptoms in some patients may not develop until a value of 6.8 mg has been reached, while in others, similar symptoms may be pronounced with serum calcium values of 8.1 to 8.3 mg.

The therapeutic correction of clinical hypoparathyroid tetany may be largely accomplished in one or more of several ways, *i.e.*, the administration of milk and calcium by mouth in conjunction with calcium salts by vein, the administration of parathormone by injection, together with calcium salts, the oral administration of vitamin D, or surgically by the implantation of parathyroid gland tissue.

The treatment of tetany with calcium alone, irrespective of the route of administration, is usually unsatisfactory due to the transient character of such therapy and incomplete relief obtained. This is due to the fact that the calcium salts, when administered orally, are irregularly absorbed from the gastrointestinal tract, and owing to poor retention (rapid urinary and fecal excretion), medication must be repeated at short intervals.

The administration of parathormone or vitamin D presupposes that a calcium-rich diet or calcium salts *per se* are used in conjunction with these agents so that an improved absorption and retention of calcium is possible. Neither of these agents alone, however, is entirely suitable for the treatment of an acute attack of tetany, in that reactions are demonstrable only after a latent period and the peak-effects occur only after nine to 12 and 36 to 48 hours, respectively. Consequently, control of clinical tetany with these agents requires careful consideration of the latent period of each agent in relation to symptomatology, as well as the total period of its effects. Another factor of clinical and, particularly, economic importance is that the patient gradually develops a tolerance to the effects of parathormone so that eventually a unit blood calcium change requires progressively larger dosages.^{15 16}

The surgical treatment of hypoparathyroidism is of temporary value only in that the degree of relief is unpredictable and the efficacy of such therapy under optimal conditions progressively diminishes after a variable period of time due to atrophic changes in the implanted tissue.

In any event, although the diagnosis of frank postoperative tetany is readily made, the establishment of the degree of an acute attack or the presence of latent tetany can be detected only by determinations of the serum calcium values. We consider the routine determination of blood calcium values both pre- and postoperatively in each patient subjected to thyroid surgery as of primary importance, for both diagnostic purposes and therapeutic control.

In the treatment of tetany, immediate alleviation of symptoms is the first

consideration at all times, but *prolonged* effective control of the tetany that maintains normal level of serum calcium, with as little discomfort to the patient as possible, is the goal sought for. We wish to report that we have used a new therapeutic agent which will definitely control tetany. This substance is a sterol—dihydrotachysterol—perfected abroad by Holtz and his associates and known as Anti Tetany 10 ("A T 10") *

Holtz¹⁷ and his coworkers, von Brand,¹⁸ Schreiber,¹⁹ and Isemer and Suchnoth,²⁰ under the direction of Professor Windaus and his collaborators Hess,²¹ Luttringhaus,²² and Holtz,²³ were among the first to observe that very large doses of "Vigantol,"²⁴⁻²⁵ a German preparation of irradiated ergosterol, led to a series of toxic symptoms, designated by some authors as hypervitaminosis D. Hypervitaminosis D has as one of its characteristic features a hypercalcemia. The main symptoms of this condition include headache, nausea, vomiting, hematuria and a moderate elevation of blood pressure. An abnormally high calcium level in the serum, over a relatively long period of time, results in the deposition of calcium salts in the heart, blood vessels, kidneys and other organs of the body.

Holtz searched for a toxic factor as a possible cause of the hypervitaminosis and found that by prolonging the irradiation of ergosterol under certain conditions he could destroy, in large part, the antirachitic factor, vitamin D, but that the "calcimose" factor was still present. Extensive investigations of the action of the 'calcimose' factor by Holtz and his associates²⁶⁻²⁷⁻²⁸ were undertaken on both normal and parathyroidectomized animals. The results indicated that this "calcimose" factor caused a marked increase in the amount of calcium in the serum of normal animals with a deposition of calcium in the organs of the body, in the parathyroidectomized animals appropriate amounts of this "calcimose" factor elevated the serum calcium to normal and prevented the symptoms of parathyroid insufficiency. Similar results were obtained in our series of patients following the development of postoperative hypoparathyroidism.

Holtz,²⁹⁻³⁰⁻³¹ and then Holtz, Gursching and Kraut,³² described this preparation which they called "A T 10" and which is now designated chemically as dihydrotachysterol. This compound, although derived from irradiated ergosterol, differs from the parent substance in that it is almost devoid of any antirachitic† action, while the calcium mobilizing factor persists and exceeds that of viosterol.

Crude irradiated ergosterol, according to our present knowledge (Fieser³³ and Friedmann³⁴), contains at least four sterols, *i e.*, tachysterol, lumisterol, dihydroergosterol, or vitamin D₂ (calciferol), suprasterol, and pyrocalciferol.

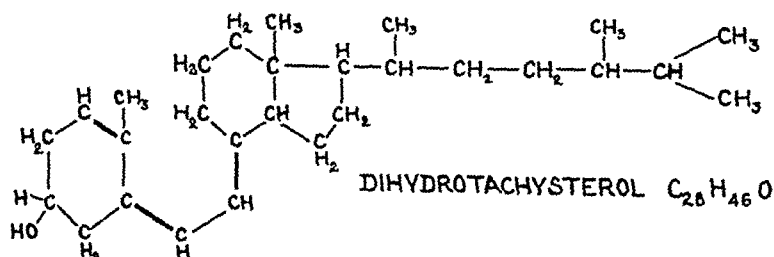
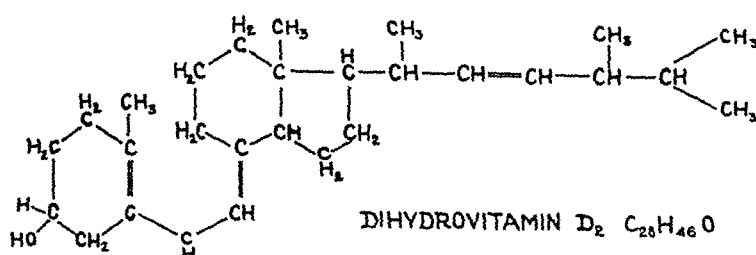
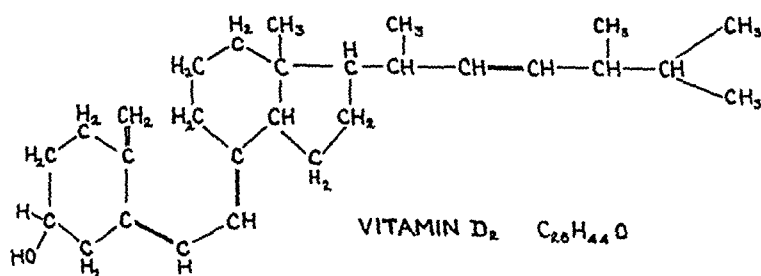
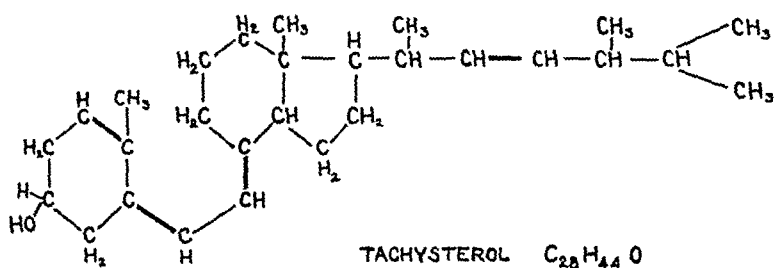
* This material has been supplied to us through the courtesy of the Winthrop Chemical Company for experimental purposes.

† Personal communication from Dr. O. W. Barlow. "The antirachitic action of 'A T 10' is approximately 1/600 of that of an equal amount of crystalline Vitamin D." We take this opportunity to thank Doctor Barlow for his many helpful suggestions and criticisms in the preparation of this manuscript.

Attention is directed to the fact that calciferol contains only one sterol Muller³⁵ states that tachysterol and vitamin D₂ (calciferol) yield identical dihydro derivatives, and consequently possess the same carbon skeleton. However, the rather striking difference in the physiologic effect of these two compounds strongly indicates that some difference exists between the points of hydrogenation of the dihydrovitamin (D₂) and dihydrotachysterol.

The following formulae show the structural relationship between the various sterol fractions mentioned in the development of dihydrotachysterol.

FORMULAE SHOWING THE STRUCTURAL RELATIONSHIPS BETWEEN THE VARIOUS STEROL FRACTIONS IN THE DEVELOPMENT OF DIHYDROTACHYSTEROL ("A T 10")



The excellent clinical results that have been reported in the literature,^{16, 36, 37, 38, 39, 40} following the use of "A T 10" in various conditions in which disturbances of calcium metabolism were present, stimulated us to make clinical tests with this new calcinose factor. Our experiences to date have been of such nature as to merit reporting. These include the oral

administration of the product in the form of a 0.5 per cent sesame oil solution of dihydrotachysterol to a series of five patients over the past two and one-half years. The subjects include three chronic and two acute post-operative tetanics following surgery of the thyroid glands performed by various surgeons. The courses of two of these five subjects, one acute and one chronic case of tetany, are herewith reported.

Case 1 (Chart 1)—Female, age 24, with a diagnosis of hyperthyroidism. Basal metabolism +31.

April 21, 1936. A subtotal thyroidectomy was performed. *Pathologic Examination*—Dr. Fred D. Bullock: "Parenchymatous and colloid goiter. It is interesting to note that imbedded in one of the lobes there is a fairly normal parathyroid."

April 22. Thyroid crisis, temperature 108°F , symptoms of tetany of a very severe form.

May 4. Calcium was 5.9 mg. Patient was given 50 units of parathyroid hormone and calcium gluconate, one ounce three times daily, with viosterol ten drops tid. From the third to fifth week, she received 50 units of parathyroid hormone daily, and the calcium varied from 5.0 to 8.7 mg.

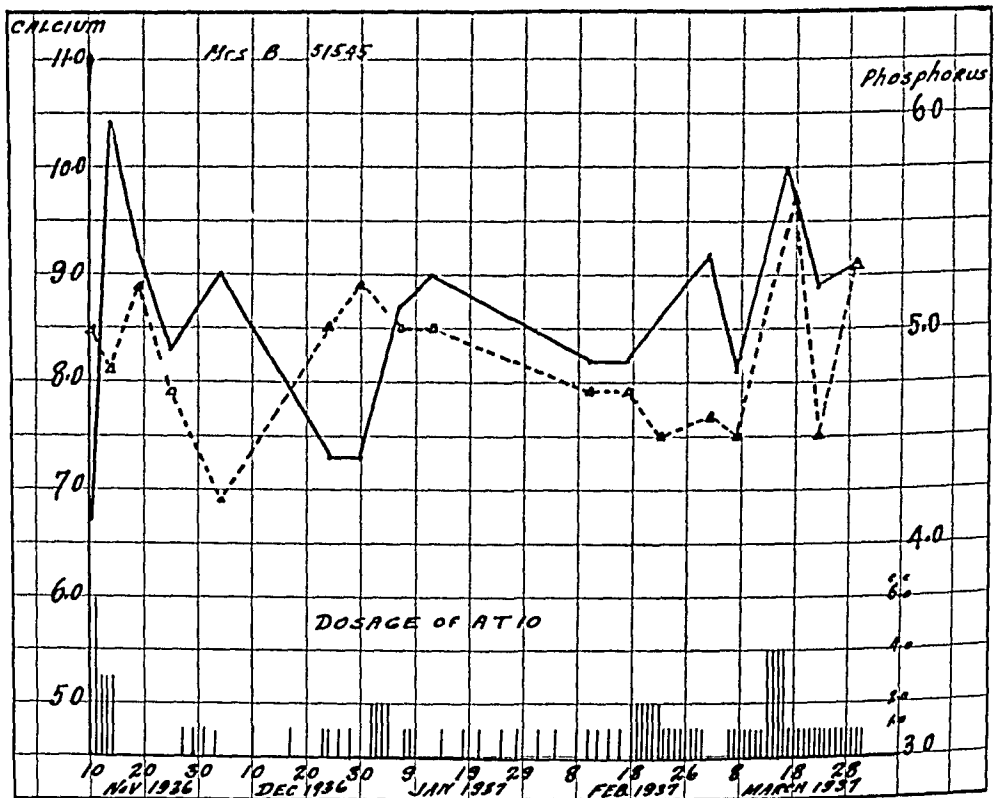
May 11. Calcium was 5.9 mg.

May 18. Calcium was 6.9 mg.

May 21. Basal metabolism -10.

Patient received parathyroid hormone until she was discharged May 23, 1936.

CHART 1



It will be noted that in spite of treatment with parathyroid hormone and calcium salts, at no time was the calcium maintained anywhere near normal.

POSTOPERATIVE TETANY

level After the patient had been discharged from the hospital, she would have to come in occasionally at night, with severe symptoms of tetany, in order to receive injections of parathyroid hormone A positive Chvostek sign was present continuously Patient had complained of tingling, sleeping of the hands and legs, and was more or less uncomfortable

In the fall of 1936 we received a supply of "A T 10," and the patient returned to the hospital to be treated for her tetany (Chart 1)

November 10, 1936 On admission her calcium was 67 mg, phosphorus 50 mg Patient was given 6 cc of "A T 10" by mouth with 45 gm of calcium gluconate divided into three doses

November 11 3 cc "A T 10" and calcium gluconate

November 13 3 cc "A T 10"

November 14 3 cc "A T 10" Calcium rose to 104 mg and the phosphorus was 48 mg At the end of 48 hours, after the "A T 10" was given, all symptoms of tetany had been alleviated with the exception of a mild Chvostek sign For the next three days, no medication was given and the calcium fell to 92 mg with a rise in the phosphorus to 52 mg

November 20-25 No "A T 10" was given, but 45 Gm of calcium gluconate per day

November 25 Calcium fell to 83 mg, phosphorus being 47 mg Patient was discharged with marked improvement in her tetany and was to receive ambulatory treatment

December 4 Patient was given 1 cc of "A T 10" every other day plus 45 Gm of calcium gluconate daily Calcium rose to 9 mg and the phosphorus was 42 mg

January 24, 1937 Patient received 1 cc "A T 10" once a week and no calcium gluconate

December 19 Patient experienced a severe shock due to the fact that her baby had been scalded to death It is remarkable to note that in spite of this she developed no symptoms of tetany

December 23 Calcium was 73 mg, phosphorus 5 mg The dosage of "A T 10" was increased 1 cc every other day plus the calcium gluconate

December 30 Calcium was 73 mg

For four days, up to January 5, 1938, she received 2 cc per day plus the calcium gluconate, and January 6, the calcium rose to 87 mg, phosphorus 5 mg

January 7, 8, 9 She received 1 cc daily plus the calcium gluconate

January 10 Calcium was 9 mg, phosphorus 5 mg

February 9 During preceding three weeks, the patient received 1 cc "A T 10" twice a week plus calcium gluconate daily

February 10 Calcium was 82 mg, phosphorus 47 mg From this period on, the amount of calcium gluconate was reduced to 1 Gm three times a day

February 17 Calcium 82 mg, phosphorus 47 mg—no change

February 18-23 Patient received 2 cc of "A T 10" daily plus 1 Gm calcium gluconate t i d

February 25 Calcium was 86 mg, phosphorus 45 mg

March 1 Patient received 1 cc "A T 10" daily

The fall in calcium without any symptoms of tetany and a very greatly diminished Chvostek sign were rather disturbing elements Examination disclosed that the patient was now two months pregnant She had not been ill with other pregnancies, but at present was very ill each day with nausea and vomiting

"A T 10" was now increased to 1 cc daily for one week, and on

March 2 Calcium was 9.2 mg, phosphorus 4.6 mg

March 3, 4, 5, 6 No "A T 10" but calcium gluconate

March 7 Calcium 8.1 mg, phosphorus 4.5 mg, patient received 1 cc "A T 10" every day for a week. She was admitted to the hospital in March, 1937, and was given 1 cc "A T 10" every day with calcium gluconate for a week.

March 13, 14, 15, 16 Patient received 1 cc of "A T 10" plus calcium gluconate

March 16 Calcium rose to 10 mg, phosphorus 5.6 mg

March 16 On advice of gynecologists, a hysterectomy was performed. No signs or symptoms of tetany occurred postoperatively.

March 17, 18, 19 Patient had received, two to three days after operation, 10 cc calcium gluconate intravenously.

March 19 Patient received 1 cc per day of "A T 10" plus calcium gluconate

March 22 Calcium 8.9 mg, phosphorus 4.5 mg

March 29 Patient discharged. She had received 1 cc of "A T 10" daily, plus calcium gluconate.

March 29 Calcium 9.1 mg, phosphorus 5.3 mg

Comment—It is interesting to note that "A T 10" alone apparently does not work as well as when given in conjunction with calcium salts, that the dosage at first was rather large—6 cc—and was decreased as soon as symptoms of tetany were lessened. However, we have also observed that the calcium rises slowly and when once the symptoms of tetany are alleviated, small doses are sufficient to maintain a normal serum calcium level, and that with any decrease in the blood calcium the dosage is somewhat increased or given over a longer period of time. The object, of course is to get the patient symptom free and to maintain a normal calcium level with as little "A T 10" as possible. This patient will probably have to take "A T 10" for a long period of time, with gradual reduction in the dosage until a normal calcium balance is established. But this is of no particular inconvenience to the patient as the substance is tasteless and, of course, given by mouth. The patient has been symptom free ever since she has taken the "A T 10".

Case 2 (Chart 2)—Female, age 32, was first seen in May, 1936, and complained of nervousness, palpitation, and loss of weight. One miscarriage six years ago was followed by loss of about 40 pounds in weight which was never regained. General health good. She was admitted to the hospital May 25, 1936.

May 26 Basal metabolism +65

June 2 Basal metabolism +73

June 8 Basal metabolism +49

June 22 Patient operated upon. Subtotal thyroidectomy. *Pathologic Examination*—Dr. F. D. Bullock. Colloid and parenchymatous goiter.

June 25 Patient developed twitching of the legs and other signs of beginning tetany.

June 26 Blood calcium was 4.9 mg, phosphorus 5.7 mg

June 27 She received 10 cc "A T 10" and 45 Gm calcium gluconate

June 28 Same dosage

June 29 Blood calcium was 5 mg, phosphorus 6.1 mg. Symptoms of tetany are considerably diminished.

June 30 Calcium 5.4 mg, phosphorus 6.2 mg

July 1, 2 Patient given 4 cc "A T 10" and 45 Gm calcium gluconate

July 3 Calcium 5.8 mg, phosphorus 6.4 mg. Very little change.

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July 3, 4, 5 Patient received 1 cc "A T 10" and 45 Gm calcium gluconate

July 7 Calcium 65 mg, phosphorus 49 mg

July 6, 7 "A T 10" discontinued, and only calcium gluconate given

July 8 One cubic centimeter "A T 10" and 45 Gm calcium gluconate

July 9 No "A T 10" and only calcium gluconate given

July 10 One cubic centimeter "A T 10"

July 11 Calcium rose to 71 mg, phosphorus 39 mg

July 13 One cubic centimeter "A T 10"

July 14 Calcium 71 mg, phosphorus 46 mg No symptoms of tetany, with the exception of a slight cramp in the leg and a mild Chvostek sign Patient discharged Basal metabolism +14 Condition good Ambulatory treatment to be continued

July 14 to August 5 Patient given 1 cc "A T 10" twice a week for one week only, plus 45 Gm of calcium gluconate

August 5 Calcium 8 mg, phosphorus 45 mg Still a mild Chvostek sign

August 4, 1936, to January 13, 1937 Patient had been placed on calcium gluconate plus calcium phosphate with a little viosterol, with the view to seeing whether serum calcium would remain above the tetany level *without* the use of "A T 10" However, serum calcium during this period, on September 3, was 9 mg and on November 18, 82 mg

January 13 Calcium had fallen to 8 mg with phosphorus 4 mg, and it was decided to give the patient some "A T 10" to stimulate calcium mobilization Patient received "A T 10," 1 cc daily, for ten days with calcium gluconate

January 26 Calcium was 83 mg, phosphorus 34 mg Dosage was continued Chvostek sign was very mild Patient feels well, no complaints

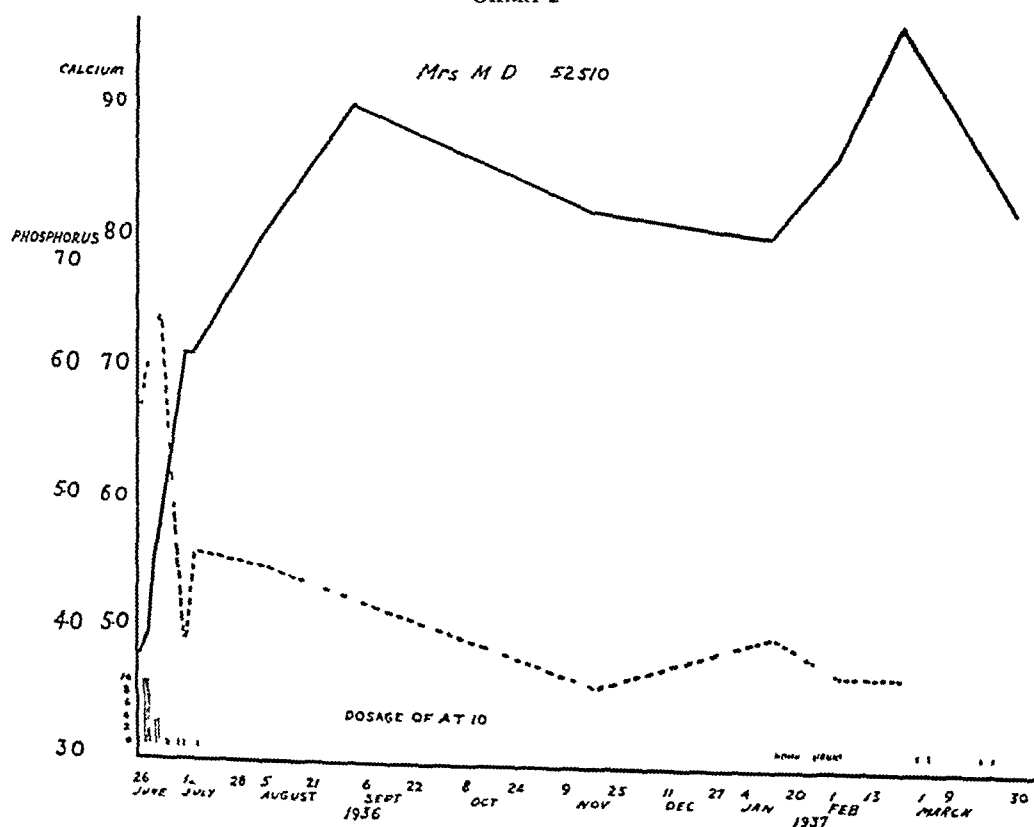
January 26 Calcium was 86 mg, phosphorus 37 mg

February 23 One cubic centimeter "A T 10" was given twice a week

February 25 Calcium was 96 mg, phosphorus 37 mg

March 30 Calcium was 82 mg No complaints, excellent condition Chvostek sign has practically disappeared

CHART 2



Comment—This case of acute tetany, in which we were fortunate to start immediate treatment with "A T 10," is of particular interest because it brings out the fact that while the blood calcium was slow in rising, her symptoms of tetany were alleviated in a very short time after administration of the "A T 10." Within 18 days, there was a marked rise in the blood calcium which was sustained with a comparatively small dose of "A T 10." During the period in which medication with the sterol was discontinued, there was a sustained normal calcium level. Of course, the question here arises as to the cumulative action of this preparation. Whether this action actually exists or not is, in our minds, open to question because as soon as "A T 10" is discontinued, there may be a fall in the blood calcium. But it can be very easily maintained by small dosages over a period of weeks. We are studying this question further. This patient has been symptom free, that is of actual tetany, ever since she has been taking "A T 10," and on the last examination was in excellent condition. This case demonstrates again the absolute necessity of determining the blood calcium and phosphorus after each period of treatment. It is only in this manner that marked deviations from normal can be observed and the figures will act as a guide for the amount of "A T 10" to be given.

CONCLUSIONS

This new therapeutic agent, dihydrotachysterol ("A T 10"), has great value in the control of postoperative tetany, and the symptoms can be alleviated within 48 to 72 hours after instituting treatment. These patients are usually irritable, extremely nervous and physically played out, and certainly the removal of these symptoms, as soon as possible is of the utmost necessity.

Therapy with dihydrotachysterol must be strictly individualized, *i e*, the blood calcium level must be carefully checked at intervals before and after medication has been instituted. Until the maintenance dosage has been determined, the amount of "A T 10," given by mouth, may vary from 1 to 3 cc every other day to 1 to 2 cc per week, depending on the severity of the deficiency. We have on occasion administered dosages as high as 10 cc daily for a period of several days, but during this period have kept a careful check on the patient's serum calcium findings. The product is not harmless and excessive dosage may well induce symptoms of hypercalcemia.

A plea is made for the routine determination of serum calcium both pre- and postoperatively in all thyroid surgery.

This new substance in our hands has been of definite value both from a subjective and objective standpoint in the control of tetany. These observations, taken in conjunction with those of Holtz and his coworkers, would suggest that dihydrotachysterol merits further chemical study and it is recommended for the treatment of postoperative hypoparathyroid tetany.

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DISCUSSION.—DR. DEWITT STETTIN (New York) felt that there was little left for him to say except to confirm in every detail what Doctors Pickhardt and Bernhard had reported so well. He was fortunate enough to have had the opportunity of observing, at first hand, some of their work, as two of the patients on whom they have reported were from his service. One of them had been shown and there was no need for him to make any further comment about her.

One of the patients to whom they had referred was a woman, age 60, upon whom Doctor Stetten had performed a left lobectomy for a large colloid goiter, October 24, 1929, and upon whom he again operated, October 17, 1933, for a similar condition in the right lobe, when a resection of part of the right lobe was undertaken. About three weeks after this second operation she developed definite, rather severe symptoms of tetany, the serum calcium dropping as low as 4 mg per 100 cc. Only with very large doses of calcium in the form of calcium gluconate, mainly intravenous, and intramuscular injections of parathormone, was she kept moderately comfortable—relieved but never well. Her calcium could never be raised much above 6.5 mg, and the phosphorus rose as high as 6 mg. At times it was necessary to give her, almost as an emergency, an intravenous injection of calcium gluconate, and

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although the tetanic spasms were relaxed promptly, they recurred often within a few hours. She managed to worry along for three years until Doctors Pickhardt and Bernhard began this work at Lenox Hill Hospital, when, on December 2, 1936, Doctor Stetten persuaded her to enter the hospital for a trial of this new agent. She did so, much against her will as she objected to further experimentation, but after a few days of treatment she was beaming and has never been able to thank him enough for having talked her into giving this drug a trial. She is really cured of her tetany, as shown not only by the complete and persistent disappearance of the carpopedal spasms, Chvostek and Trousseau signs, but also by a serum calcium that is practically normal, and the characteristic drop in the blood phosphorus—and that with only relatively small doses of the drug by mouth at comparatively long intervals, supplemented by moderate amounts of calcium also administered orally. She has even been able to resume her occupation as dressmaker. Whatever "A T 10" or dihydrotachysterol is or in whichever way it produces its result, it is certainly a calcium fixative, and, as such, apparently controls postoperative parathyroprival tetany. The effect of the administration of this agent in this distressing disturbance is most dramatic—really little short of miraculous—and Doctor Stetten does not think he is exaggerating when he states that, in its more limited field of application, it is only comparable to the specific actions of insulin in diabetes or liver extract in pernicious anemia.

Doctor Stetten feels that the Society is under a great debt to Doctors Pickhardt and Bernhard for introducing this drug into America, for so carefully studying its action, and for so convincingly presenting to it this evening, the results of their research.

CONGENITAL DIAPHRAGMATIC HERNIA*

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DIAPHRAGMATIC hernia is a protrusion of the abdominal organs into the chest through a defect in the diaphragm. In the congenital type, with which this paper deals, the defect is usually caused by a failure of fusion in the various parts of the embryonic diaphragm, and the herniated organs may lie free in the chest with or without a peritoneal sac. Infrequently, herniae occur after fusion has taken place when the increase in the abdominal pressure causes a protrusion through some weak area. In the latter type, a peritoneal sac is more likely to be present than in the former.

It is still difficult to estimate the incidence of congenital diaphragmatic hernia because of the variance of published reports. In 1610 Ambroise Pare reported two traumatic cases. In 1769, Morgagni wrote the first monograph on the subject. In 1920, MacMillan¹⁸ found only three cases among 15,000 roentgenologic examinations, and in 1924 Pancoast and Boles²² reported 16 cases among 9,000 gastro-intestinal examinations. In 1931, Hedblom¹² collected 1,435 cases from the literature. In 1933, Dickson⁷ reported 206 cases during the preceding 14 years from the roentgenologic department of the Toronto General Hospital. Harrington,¹¹ in 1933, stated that they had had five times as many cases at the Mayo Clinic during the preceding eight years as they had had during the previous 24 years. The purpose of this paper is to record ten cases of the congenital type from the Babies Hospital, New York, seen during the past seven years.

The most common sites of the defects in the diaphragm through which the abdominal organs pass are The foramen of Bochdalek, the foramen of Morgagni, the dome of the diaphragm, and the esophageal hiatus. It is interesting to note that a hernia through the aortic or vena caval openings in the diaphragm has never been reported.

Embryology—The diaphragm is so complex in development that it is not difficult to understand how a defect may arise where the different segments meet. The embryonic diaphragm consists of two parts: a ventral part which is the cephalic portion of the septum transversum, developing in the cervical region, and a dorsal part which is the pleuroperitoneal membrane, developing from the lateral body walls and destined to become the closing membrane between the pleural and the peritoneal cavities. The muscular portion of the diaphragm develops while it is in the cervical region from the third and fourth cervical myotomes on each side. During development, the diaphragm migrates from the region of the third cervical vertebra to its final location opposite the

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twelfth thoracic vertebra, and, during this migration, its plane of direction changes many times. It is thought that the original communication between the pleural and peritoneal cavities closes about the third month of intra-uterine life. If this communication remains open, there is formed the pleuro-peritoneal hiatus known as the foramen of Bochdalek. Since the liver lies over the right foramen, herniae at that point occur less often than on the left side. Failure of fusion of the costal and sternal fibers at either side of the sternum results in the formation of the foramina of Morgagni. It is more difficult to explain the defects in the dome of the diaphragm from an embryologic standpoint, other than to say that they are due to a failure of fusion of the elements at that point. The defects in the dome are more common on the left side. Hernia through the esophageal hiatus has been attributed either to the failure of development of the diaphragm at that point, or to the failure of migration of the stomach because of a short esophagus. These herniae usually have a peritoneal sac.

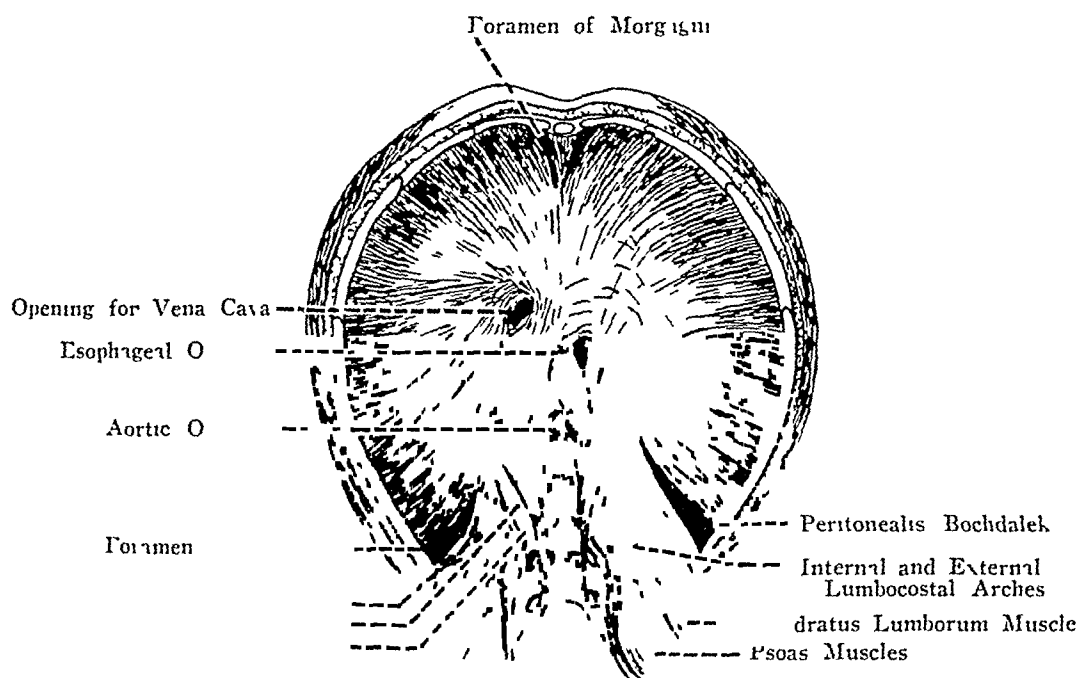


Diagram showing the location of the more common defects in the diaphragm. (Reproduced from Hermann, W. G. *Radiology*, 22, 241-246, February, 1934.)

Symptomatology—The symptoms of diaphragmatic herniae, which are the result of mechanical interference with the functions of the herniated viscera and of interference with the respiratory and circulatory organs upon which they encroach, may be respiratory, gastro-intestinal or a combination of both. If the herniated viscera press upon the heart or mediastinum, they may produce cyanosis, dyspnea and palpitation. If they consist of large or small intestine, nausea, vomiting or an intestinal obstruction may result from the crowding or kinking of the intestine. The symptoms vary to such a marked degree that the possibility of diaphragmatic hernia should always be kept in mind in cases exhibiting perplexing upper abdominal, respiratory or cardiac symptoms.

the etiology of which is difficult to ascertain. Many cases are symptom-free, and the hernia is discovered during the course of routine roentgenologic examination. One patient, whose condition was discovered after taking a roentgenogram of her chest, had been so well that it was difficult to convince her parents that a serious condition existed. Shortness of breath during the hot days of July was the only complaint of another. One patient suffered from loss of weight and vomiting since birth, while another had had a cough, diarrhea and tarry stools for several weeks.

Diagnosis—The diagnosis of diaphragmatic hernia is greatly facilitated by roentgenologic examination. A roentgenogram of the chest will often show gas bubbles in the place of normal lung and frequently a displacement of the heart. Previous to 1900, when opaque media were first used to roentgenograph the gastro-intestinal tract, most of the diaphragmatic herniae were discovered at autopsy. Roentgenologic examination probably has been the greatest factor in the improvement in diagnosis and treatment of these cases. Not only does it identify the herniated structures, but it often demonstrates the location of the defect in the diaphragm.

Time for Operative Intervention—Operative repair is practically the only relief for this condition. If the herniated contents contain any portion of the small or large intestine, operation should be advised immediately, especially in young children who evidence symptoms of impending obstruction, which is the most urgent indication. We were unfortunate enough to have a five weeks old baby (Case 4) develop a high intestinal obstruction while we were attempting to improve its general condition preparatory to operation. Another reason for not deferring operation is that, if the abdominal contents are allowed to remain in the chest for a long period, the development of the abdomen will be so retarded that it may not be large enough to accommodate the structures brought down into it from the chest. We had this experience with one of our patients (Case 5).

Operative Approach—Opinions differ relative to the surgical approach in these cases. However, I prefer the abdominal approach, and have employed a subcostal incision in each case. In one instance of recurrence, it was necessary to make a thoracic incision in addition to the subcostal. The subcostal incision gives an excellent approach to the diaphragm, and it has always seemed easier to me to reduce the structures by traction from below than by forcing them down from above. The abdominal approach also lessens the occurrence of thoracic complications, and it gives one an opportunity to rearrange the abdominal contents to as near their normal position as possible. There are many advocates of the thoracic approach, notably TUESDALE,²⁶ who recommends it in all cases. HARRINGTON prefers the abdominal approach, and HEDBLUM believed that both the thoracic and the abdominal approaches had their special advantages and limitations, depending upon the anatomic and clinical type of hernia.

My experience with this small group of cases leads me to believe that it is desirable to expose the phrenic nerve in the neck before making the abdominal incision so that the nerve may be crushed if paralysis of the diaphragm seems advantageous after the hernia has been exposed. If the thoracic approach is employed this procedure is unnecessary, because the nerve may be crushed in the thorax. Positive pressure anesthesia is decidedly advantageous, and it was employed in most of my cases.

I believe these patients should be kept in an oxygen tent for several days after operation. Not only does the oxygen decrease the respiratory effort, thereby saving the child's energy, but the tent decreases the chances of respiratory infection because the temperature can be so easily regulated. Pleural effusion may follow operation, and if it occurs, the chest should be aspirated as often as the quantity of fluid demands.

The difficulties of the operation depend upon the location of the defect and the presence of adhesions, while the mortality depends to a large extent upon the age of the patient. Hedblom found that in 210 cases under one year of age, 75 per cent died before they were one month old. All but one of the operated cases here reported were under six months of age.

CASE REPORTS

Case 1—P. N., male, age $4\frac{1}{2}$ months, was admitted to the Babies Hospital, October 11, 1930, with the history of having had difficulty in breathing during the hot weather. He had had a convulsion 24 hours before admission. Otherwise, he was perfectly well. Roentgenologic examination showed small intestine in his left chest.

Operation—The abdomen was opened through a left subcostal incision which revealed a hernia through the left foramen of Bochdalek. His chest contained all of the small intestine beyond the duodenojejunal juncture, all of the colon to a point beyond the splenic flexure, and the spleen. The splenic flexure of the colon was adherent to the parietal pleura, and it had to be mobilized before it could be brought down. All structures were, however, reduced, and the diaphragmatic opening was closed with mattress sutures of black silk, the edges of the hiatus being overlapped. The patient was kept in an oxygen tent and had a continuous intravenous drip of saline for several days postoperative. His convalescence was uneventful.

Follow-Up—Six and one-half years postoperative, the child was normal in every way.

Case 2—S. D., female, age 6 months, was admitted to the Babies Hospital, November 13, 1931, with a history of vomiting during the preceding five days. Full term birth by cesarean section. She had gained steadily, and had had no illness previous to the present one. She was a well developed, well nourished, white female child. A gastro-intestinal series showed small and large intestine in the right chest.

Operation—November 20, 1931. The abdomen was opened through a right subcostal incision. On retracting the liver from the diaphragm, a patent foramen of Bochdalek was revealed behind it. The chest contained the third and fourth parts of the duodenum, all the small intestine, and all of the large intestine as far as the midtransverse colon. The structures were reduced, and the opening closed with mattress sutures of black silk. Convalescence was uneventful.

Follow-Up—Roentgenologic examination six years postoperative shows the lung



FIG. 1.—Case 1. Hernia through the left foramen of Bochdalek. Small intestine in the left chest. Heart displaced to the right. Left lung collapsed.

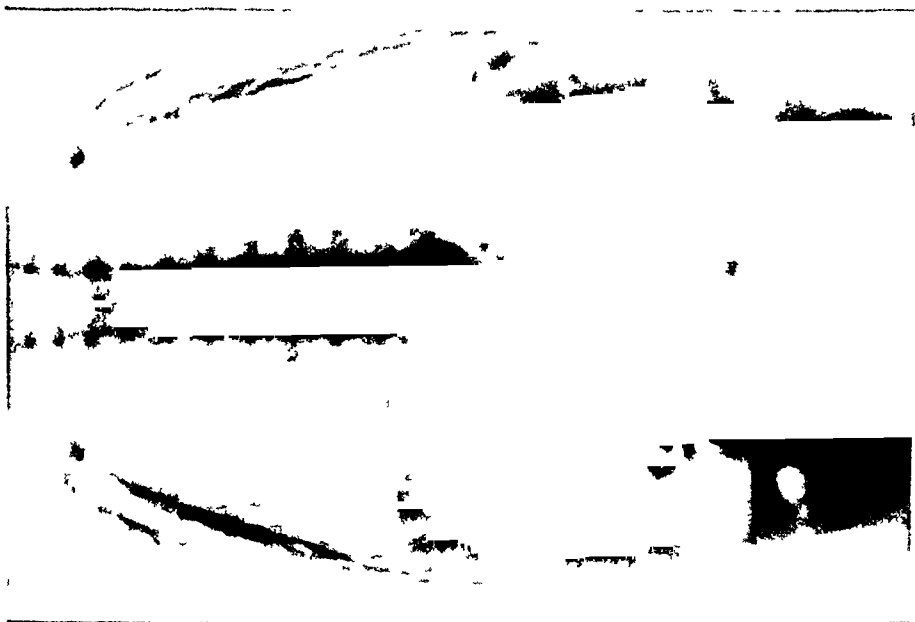


FIG. 2.—Case 1. After operation. Left lung expanded. Heart in normal position.



FIG. 3.—Case 1. After operation. All abdominal structures below the diaphragm.

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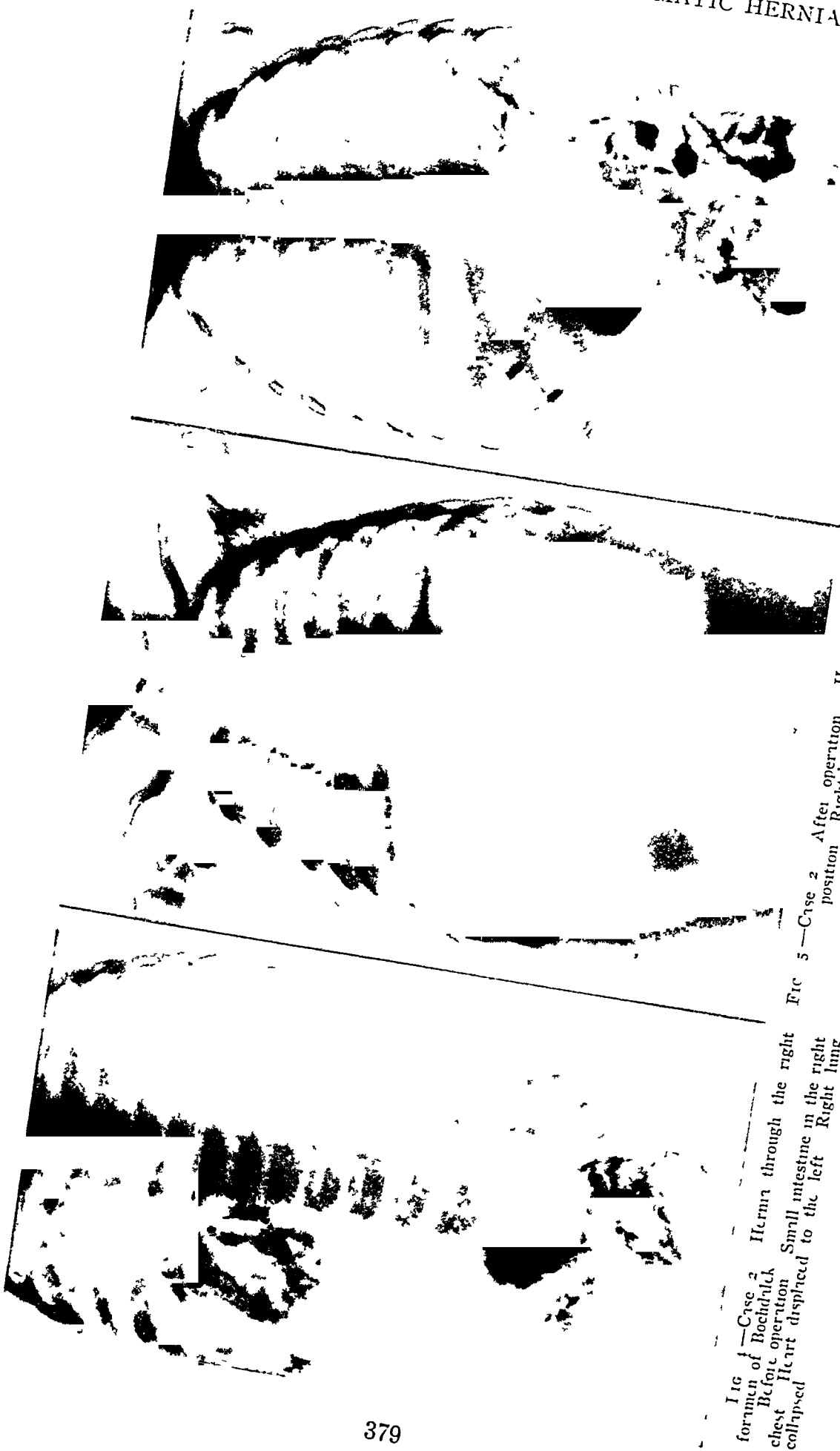


Fig 1—Case 2
foramen of Bochdalek
chest Before operation
collapsed Heart displaced to the left Right lung

Fig 3—Case 2 After operation
position Right lung expanded
Heart in normal

Fig 6—Case 2 All abdominal structures below
the diaphragm

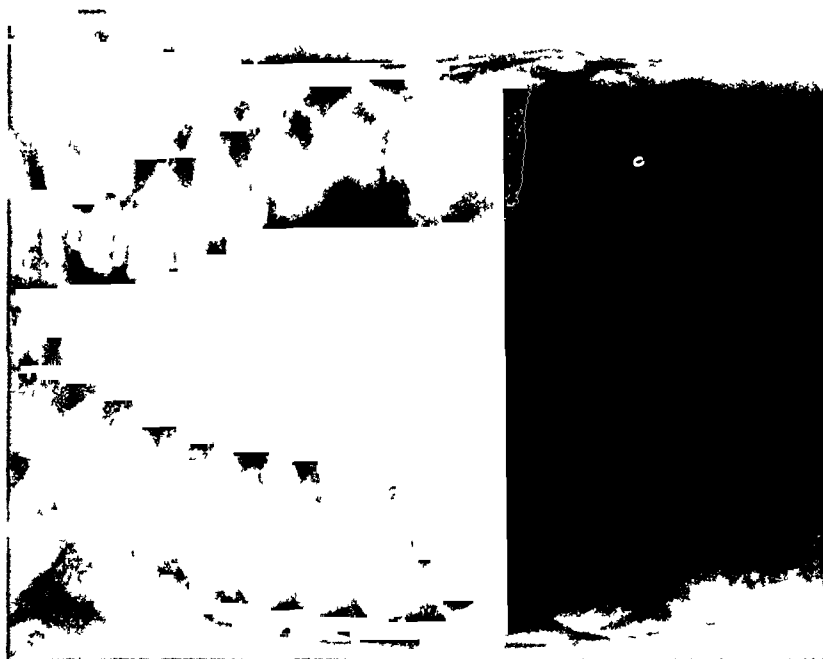


FIG. 9—Case 3. One year after repair of recurrence. Heart in normal position. Right lung expanded. Abdominal structures below the diaphragm.



FIG. 8—Case 3. Recurrence one and one half years later. Heart displaced to the left. Right lung collapsed. Small intestine in the right chest.

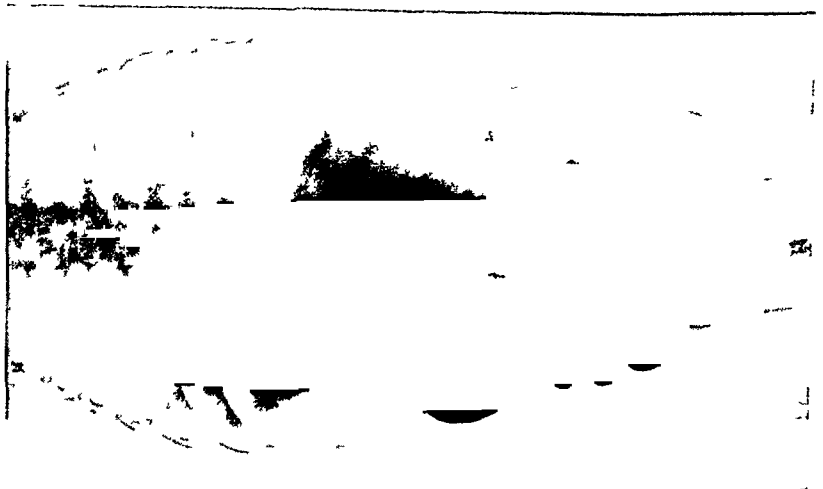


FIG. 7—Case 3. Hernia through the right foramen of Bochdalek. Before operation. Colon in right chest. Heart displaced to the left. Right lung collapsed.

expanded, and all abdominal structures below the diaphragm. The child has been very well.

Case 3—A E, male, age 5 months, was admitted to the Babies Hospital, March 13, 1934, with a history of dyspnea and cyanosis since birth. Roentgenologic examination showed small and large intestine herniated into the chest through a defect in the right diaphragm.

Operation—The abdomen was opened through a right subcostal incision, and disclosed a defect in the posterior half of the right diaphragm, which corresponded to about one-half the size of the entire right leaf. Closure seemed impossible. The structures in the chest consisted of all of the small intestine beyond the duodenojejunal junction, the cecum, the appendix and right half of the transverse colon, and the right kidney. All viscera were, however, reduced, and the defect closed with considerable difficulty. Convalescence was uneventful.

The patient remained free from symptoms for about one and one-half years, when a routine roentgenogram of his chest, October 29, 1935, showed a recurrence.

Second Operation—Age 2½ years. Twenty-four hours before repair, under avertin anesthesia, the right phrenic nerve was exposed in the neck, a loop of plain gut placed about it for traction, so that it could be readily identified and crushed if necessary. Under ether anesthesia, 24 hours later, the scar of the right subcostal incision of the previous operation was excised, and the abdomen opened. Practically all of the structures that were in the chest at the time of the first operation had reherniated into it. There were many adhesions present, and reduction of contents necessitated considerable dissection. In order to close the defect, a right intercostal incision was made through the eighth space, which greatly facilitated the closure of the diaphragmatic defect. The phrenic nerve was then crushed from within the chest. Closure was accomplished with mattress sutures of black silk. The patient developed pneumonia and pleural effusion in the right chest postoperatively, 275 cc of sterile fluid were removed from the right chest upon two occasions.

Follow-Up—It is now one year since the second operation, and roentgenologic examination, April 13, 1937, shows that the right lung is completely expanded, the heart is in normal position, and all of the abdominal viscera are below the diaphragm.



FIG 10—Case 4. Hernia through the right foramen of Bochdalek.

Small intestine in the right chest. Heart displaced to the left. Right lung collapsed. Marked distention of the stomach and duodenum by gas is also to be seen extending to the first segment of the jejunum, from which one may infer the existence of an obstruction in this location, and which condition was substantiated at operation.

Case 4—M B, male, age 5 weeks, was admitted to the Babies Hospital, January 6, 1936, with a history of vomiting and cyanotic episodes for two days "Was developing well until two days ago when he collapsed, turned blue and had rapid respirations" Had a similar spell 24 hours before admission He had been delivered by cesarean section Roentgenologic examination showed the right chest filled with small intestine While under observation, the patient developed a high intestinal obstruction and was immediately operated upon

After isolation of the phrenic nerve in the neck, a right subcostal incision was made A large, posterolateral defect was found in the diaphragm through which practically all of the small intestine had herniated into the chest A definite obstruction, due to a kink was found in the upper jejunum The opening in the diaphragm was closed with mattress sutures of black silk The patient was placed in an oxygen tent immediately after operation but he died 12 hours later as the result of shock



FIG 11—Case 5 Hernia through the left foramen of Bochdalek, and a defect in left dome of the diaphragm

Gas bubbles in the left chest Left lung is collapsed

FIG 12—Case 5 Colon in the left chest, and very greatly dilated

There was no choice but to operate upon this case A palliative operation could not be performed because of the high intestinal obstruction This is a serious complication, and one which may happen in any case where there is either small intestine or colon in the chest This patient also had an umbilical hernia, bilateral cryptorchidism, penile hypospadias, hypertelorism, and a pilonidal sinus

Case 5—F C, male, age 10 months, was first admitted to the Babies Hospital, in 1924, with the history of vomiting and convulsions Roentgenologic examination showed the whole left chest filled with small intestine He was discharged but was readmitted several times subsequently, with signs of an intestinal obstruction Each time he was taken home against advice, when his obstructive symptoms had disappeared He was finally admitted, when eight years old, with obstructive symptoms, at which time his parents consented to an operation

Fig. 13—Case 6. Hernia through the esophageal hiatus. Before operation stomach is in the chest. Esophagus is short. Transverse colon also found in the chest at operation.



Fig. 14—Case 6. Three months after operation. Small part of the stomach has reherniated into the chest. Esophagus appears to be short.



Fig. 15—Case 6. Transverse colon is entirely below the diaphragm.

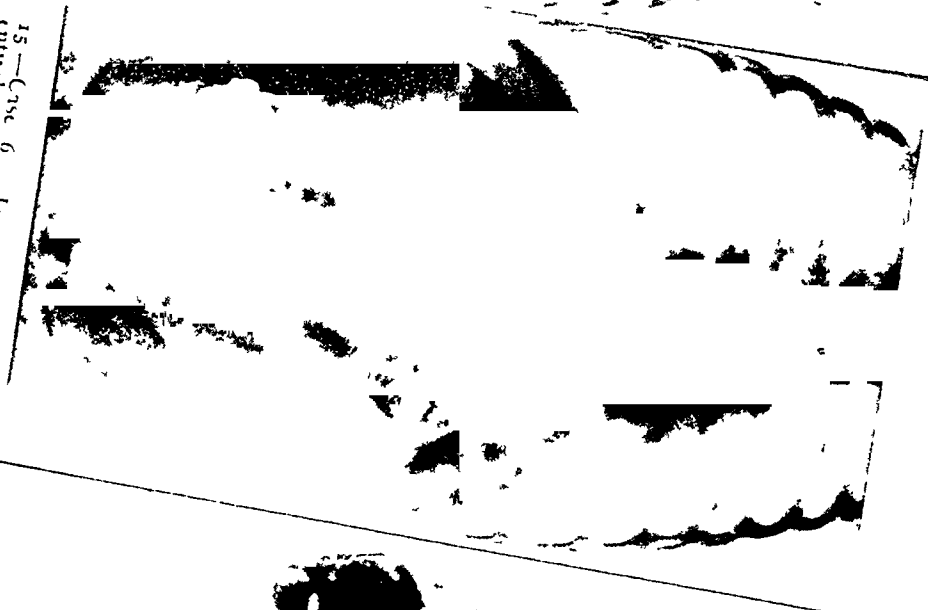


Fig. 16—Case 6. Lateral view showing upper end of colon with contrast medium.



Operation—April 25, 1932 The abdomen was opened through a left subcostal incision, which revealed a patent, left foramen of Bochdalek as well as a defect in the left dome. The left chest contained all of the small intestine from the duodenojejunal juncture on, all of the colon to a point beyond the splenic flexure, and the spleen. The structures were removed from the chest after a very tedious dissection. Both openings in the diaphragm were closed with mattress sutures of silk. The structures could not be returned to the abdomen because they had never been there before, and the cavity was not large enough to contain them. The child's condition was desperate in spite of a transfusion and an infusion on the operating table. His condition was so precarious, that the defects in the diaphragm were reopened and the viscera replaced into the chest. The patient died three hours postoperative. He should have been operated upon earlier in life, as his abdomen was not sufficiently developed to contain

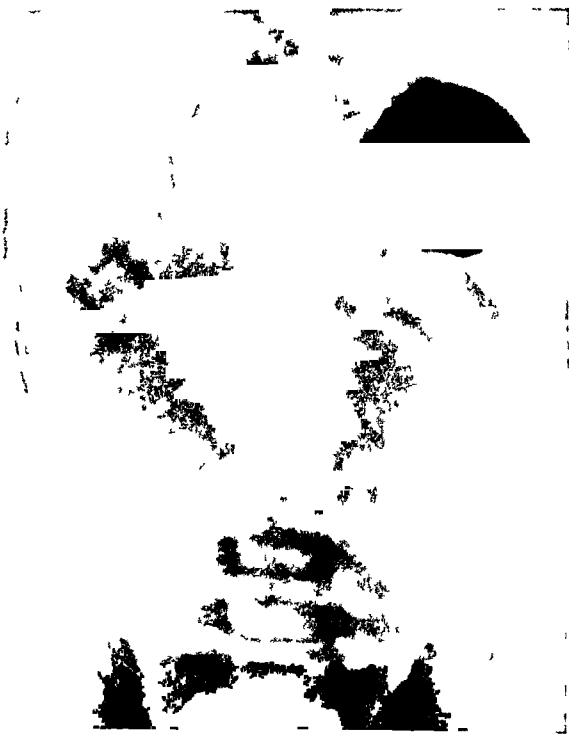


FIG 17—Case 7 Hernia through the esophageal hiatus
No operation Stomach in the chest

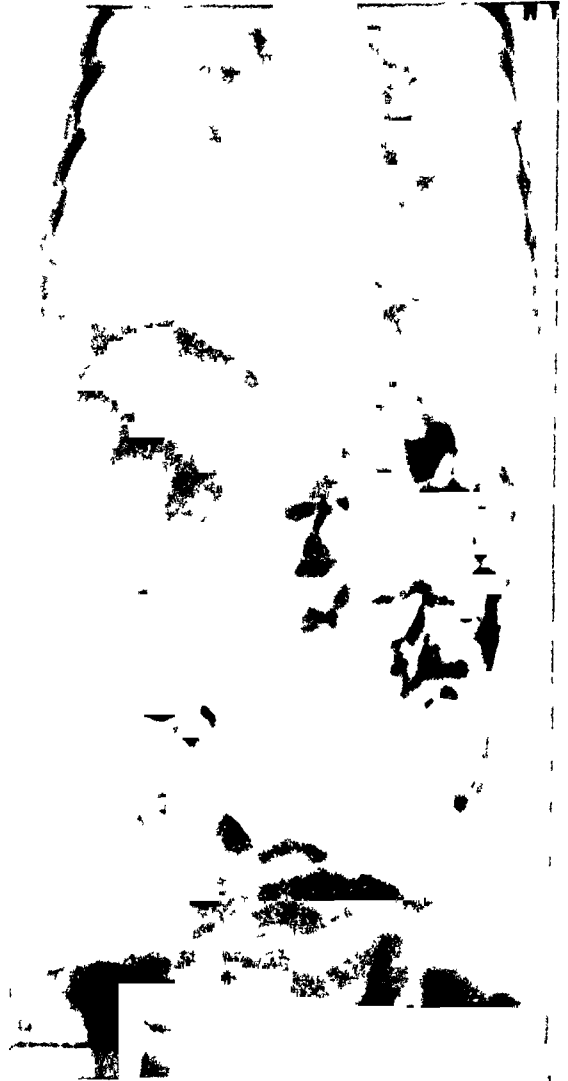


FIG 18—Case 8 Hernia through the esophageal hiatus
No operation A large part of the stomach had herniated into the chest through the esophageal hiatus

the viscera removed from his chest, in addition he should have had the phrenic nerve crushed before operation.

Case 6—L Y, female, age 6 months, was admitted to the Babies Hospital, June 22, 1931, with a history of loss of weight and vomiting for three months. She was a pale, undernourished child, whose roentgenologic examination showed her stomach and transverse colon herniated into her chest through the esophageal hiatus. She continued to vomit while under observation for two weeks. The vomitus contained blood on several occasions.

Operation—July 8, 1931 The abdomen was opened through a right subcostal in-

CONGENITAL DIAPHRAGMATIC HERNIA

cision The entire stomach, the first and second portions of the duodenum and almost all of the transverse colon were found to be in the chest, having herniated through a large esophageal hiatus The viscera were reduced, and the esophageal hiatus was closed tightly around the esophagus after a large stomach tube had been passed It was evident at operation that the esophagus was short, as it was only with considerable traction on the stomach that it could be kept in the abdomen Convalescence was uneventful

Roentgenologic examination, three months later, showed that a small portion of the stomach had reherniated into the chest The patient has not been examined during the past year, but was doing well when last heard from This was about the result we



FIG 19—Case 9 Hernia through the foramen of Morgagni
Part of the transverse colon in the chest having herniated through the right foramen of Morgagni

FIG 20—Case 9 Showing how helpful lateral view may be in demonstrating the location of the defect in the diaphragm

expected in this case At least the operation kept the transverse colon from reentering the chest

Case 7—S N, female, age 3½ years was admitted to the Babies Hospital, November 16, 1932, with the history of paleness, and refusal of food and vomiting The child had a wax pallor, pale mucous membranes, and a systolic murmur at the apex While under observation, she had a large hematemesis, and was transfused immediately Her condition improved rapidly, but her mother refused to have the child operated upon, and took her home against advice

Roentgenologic examination showed the stomach above the diaphragm Follow-up disclosed that the patient died of pneumonia during the past year

Case 8—D S, age 2 months was admitted to the Babies Hospital, October 10, 1933 suffering chiefly from malnutrition This child also had a complete cleft palate

Roentgenologic examination showed the stomach in the chest, having herniated through the esophageal hiatus. The patient was taken from the hospital against advice, without operation. Follow-up report one month ago, stated that the child was doing very well.

Case 9—J. H., male, age 3 months, was admitted to the Babies Hospital, April 1, 1932, with a history of cough and fever for the past two weeks. The child was pale, poorly developed, poorly nourished, and typical in every way of a Mongolian idiot. Roentgenologic examination showed bilateral bronchopneumonia. A later gastrointestinal series showed a large part of the colon to have herniated into the right chest through the foramen of Morgagni. He developed diarrhea and intestinal hemorrhage, and died without operation.



FIG. 21. Case 10. Hernia through the foramen of Morgagni. Part of the colon in the chest to the right of the sternum.

Case 10—R. D., age 11 months, was admitted to the Babies Hospital, February 3, 1937, with a history of shortness of breath since the age of two months. The patient had always been a feeding problem, and was a typical Mongolian idiot. Roentgenologic examination showed a herniation of the colon through the right foramen of Morgagni. There was a definite upper respiratory infection present and the child was discharged because of this, but is to return for operation.

Results—In this group of cases, seven operations were performed upon six of the ten patients. One case is to be operated upon when he recovers from a respiratory infection. Two patients died from shock, one, a five weeks old infant who developed a high intestinal obstruction while being prepared for operation, and the other, a boy, age 8, died after a long and tedious dissection of structures adherent in the chest and the closure of two diaphragmatic defects. One case of esophageal hiatus hernia has a partial recurrence due to a short esophagus, but he is doing well. One patient operated upon

at the age of five months had a recurrence one and one-half years later The operation for recurrence seems successful, two years later One case with hernia through the left foramen of Bochdalek is well seven years after operation One case with hernia through the right foramen of Bochdalek is well six years after operation

Five of these ten patients showed no congenital abnormalities other than the diaphragmatic hernia Both patients with herniae through the foramen of Morgagni were Mongolian idiots One of these also had a congenital heart derangement One case of esophageal hiatus hernia had a cleft palate One patient (Case 4) also had an umbilical hernia, bilateral cryptorchidism, penile hypospadias, hypertelorism and a pilonidal sinus

SUMMARY

(1) The symptoms of diaphragmatic hernia may be either respiratory or gastro-intestinal in origin, depending upon what viscera are contained in the hernia and what structures in the chest are pressed upon by the hernial contents

(2) Many cases of diaphragmatic hernia are symptom-free and are discovered in the course of a routine roentgenologic examination

(3) The diagnosis of diaphragmatic hernia is most surely arrived at by a roentgenologic study

(4) Treatment should be surgical repair of the hernia in all cases where any portion of the intestinal tract is involved, because of the danger of intestinal obstruction

(5) The author prefers the abdominal approach, but there are many surgeons who prefer the thoracic approach

(6) Positive pressure anesthesia is very desirable

(7) Patients should be placed in oxygen tents after operation

(8) Pleural effusion may occur after operation, and should be aspirated

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DIRECT INGUINAL HERNIA *

PRESENTATION OF AN OPERATION FOR ITS CURE

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HALSILD¹⁴ states that an operation for the cure of inguinal hernia was devised and published by Heliodorus who lived during the time of the Roman Empire. This operation corresponded to some extent to operations performed during our time.

The Bassini Operation—It was not, however, until Bassini^{5, 23} devised his operation, in 1884, that a procedure was presented which was based upon exact anatomic studies. The earliest description of this operation that I have been able to find was that published, in 1890, in the *Archiv für klinische chirurgie*, Berlin. In this he referred to the work of Wood, von Segond, von Lucas-Championniere and Czerny, all of whom had devised operations for the cure of hernia. He states that Julliard had only a single radical cure in 22 operations. It seems that following all of these operations the patient needed to wear a truss to prevent recurrence. He himself first operated by the Czerny method, in which the sac was dissected out and cut away after tying its neck with catgut. The neck was then thrust into the abdominal cavity and the wound closed with catgut sutures. He undertook to improve results by devising first an operation which was similar to the one devised by Macewen about the same time, in which after ligating and excising the sac, the neck was sutured under the aponeurosis of the external oblique, and the process of the neck beneath the ligation was gathered up with sutures to form a pad which was supposed to be a bulwark against any further descent of hernia. Subsequent investigations showed him that this pad was quickly absorbed, and his operation was no better than that of his predecessors. He then devised the operation in 1884 which has since borne his name. After having described the operation he states the principle of it as follows: "In both cases, that is in external (acquired or congenital), or in internal (direct) herniae, the inguinal canal is reconstructed after the manner of its physiologic formation, that is, with an abdominal and subcutaneous opening, of which the first lies external to the second, and is provided with two walls, one posterior and the other anterior. Under the influence of abdominal pressure, the new posterior wall is pressed against the anterior and both support each other in order to withstand the continuous and strong impulse of the abdominal viscera, while the spermatic cord is permitted to pass through between them. The new abdominal opening and the new posterior wall of the inguinal canal are formed from muscular and aponeurotic tissues which functionate and therefore cannot disappear by resorption."

Recurrences—It is interesting to note that in our country the failure to

* Read before the Southern Surgical Association, Birmingham, Ala., December 9 1937.

secure a radical cure by operations in vogue previous to the Bassini type is set forth in a statement by Dr W. T. Bull, as quoted by Halsted "Now [1890] that ten years have elapsed since the modern radical operations have been in vogue, we ought to hear of, or have presented to us patients who have been more than five years at the least, without relapse. We could naturally expect to see such cases occasionally, but there are none such."

Other Operative Procedures—Wm. S. Halsted devised his operation in 1888,¹⁰ and first published his results, as far as my researches go, in 1893. Alexander H. Ferguson,¹⁰ in his first paper published in 1895, reported an operation in which he followed the technic of Macewen in plicating the sac to the inner surface of the abdominal wall to block another descent of the hernia. The cord was placed external to the aponeurosis of the external oblique. His second operation,¹¹ and the one that bears his name, was published in 1899.

Without contrasting the merits of these three operations, Bassini, Halsted and Ferguson, they are all sufficiently alike to suggest a common origin. They all provide for the complete removal of the sac and the reconstruction and reinforcement of the abdominal wall. Their chief difference is in the method of dealing with the cord. It would appear that the suggestion for the methods of Halsted and Ferguson was from Bassini's operation. There can be no question of the value of these methods, and the large number of cases permanently cured by them is a sufficient testimony in their behalf.

However, there were more or less numerous recurrences reported by various surgeons, and the reasons for this and the various methods suggested to overcome recurrence, have given rise to a voluminous mass of surgical literature. It seems to be generally conceded now that where there is recurrence after the neck had been properly ligated and the sac removed, it occurs below the abdominal opening of the canal.

Operations Designed to Prevent Recurrence—The following are some of the principal methods adopted to prevent recurrence.

In 1901, L. L. McArthur¹⁹ reported his operation for strengthening the suture line between the muscles and conjoined tendon and Poupart's ligament by the use of strips of fascia derived from the pillars of the external ring and extended up to the belly of the external oblique muscle. In 1904, he²⁰ reported again on the same operation.

In 1906, E. W. Andrews³ reported on imbrication of the aponeurosis of the external oblique.

In 1920, Hoguet¹⁵ reported on folding back the medial flap of the aponeurosis and including that in the sutures of the muscle to Poupart's ligament, after which the edge of this flap was sutured to the lateral flap over the cord.

In 1924, Edmund Andrews^{1, 2} reported on exposing the thickened part of the transversalis fascia and suturing that to Poupart's ligament.

There have been many other procedures advocated, but those mentioned above express the general ideas.

Other Explanations of Recurrence—Another explanation of recurrences was that offered by Seelig and Chouke,²⁵ in 1923. They made the contention that muscle sutured to fascia did not unite with it, but that what took place was simply an adhesion which becomes attenuated under pressure. Still another explanation was that suture of muscle was harmful.

In 1923, Sir Arthur Keith¹⁷ described the shutter action of the muscles surrounding the inguinal canal by which these muscles contract and close the canal to counteract pressure from above.

In 1925, R. Hamilton Russell²⁴ advocated proper removal of the sac alone in the cure of simple indirect hernia. This had been his practice in operating at a children's hospital and he had extended the operation to include younger adults before deformity and distortion had taken place. He was of the opinion that suture of the muscle injured it and prevented its action and predisposed to recurrence.

In 1933, J. D. Rives²² expressed the same opinion and gave three cardinal principles as follows: (1) Muscle deprived of function atrophies, (2) muscle offers no considerable resistance to forces directed perpendicular to its fibers, (3) fascia must be applied directly over the defect. For this purpose he advocated the Andrews imbrication.

All of these have a basis of sound reasoning, and of all the modifications, Seelig's (1927) method²⁶ of applying the McArthur fascial suture appears to me to be the best. However, no operation that depends for its permanency upon the suture of muscle or fascia to Poupart's ligament will be uniformly successful in the cure of all types of inguinal hernia.

The Chief Reason for Recurrence—This weakness consists of the absence of a well-formed conjoined tendon and attenuation of the muscles that form it. It is to this point that I wish particularly to draw attention.

The difficulties encountered in effecting a cure of direct hernia by the methods referred to, the reasons for recurrence, and the presentation of an operative procedure, which in my hands, thus far, has effected cures in 100 per cent of 27 operations, is the object of this paper. That the methods commonly in use have a high percentage of recurrence is shown by many published reports, of which the statistics given in Christopher's Surgery,⁷ published in 1936 (page 1376), are a fair sample. The section on hernia is written by Seward Erdman and he states: "From a number of the largest and best surgical clinics follow-up reports based on actual examinations show from three to seven per cent recurrence after operations for indirect hernia, and from 15 to 30 per cent after operations for direct hernia."

That there is a defect at the point where direct hernia occurs was early discovered by Bassini, but the methods that he advocated for overcoming this were ineffectual. Halsted, and Bloodgood⁶ endeavored to fill in this defect by suturing the rectus muscle or a flap from its fascia to Poupart's ligament, and W. A. Downes⁸ advocated the same procedure. However, in a later paper he states: "The problem of inguinal hernia resolves itself into the

management of the direct variety. I have personally reached the conclusion that a certain number of direct hernia cannot be cured by operation."

Joseph C. Bloodgood states: "The chief cause of recurrence in the lower angle of the wound, stated in a previous report of operations at Johns Hopkins Hospital, in 1899 was due to the fact that, whether the hernia was direct or indirect, the conjoined tendon was weak or obliterated and the ordinary suture or closure of the defect in the abdominal wall was not sufficiently strong to protect from recurrence in the lower angle, and that the transplantation of the rectus muscle and its fascia was not a certain cure."

Diagnosis of Direct Hernia—In diagnosing direct hernia, the scrotum is invaginated by the examining finger which passes directly over the pubic bone into the pelvic cavity. Sometimes two fingers can be introduced and swept freely around the inner walls of the pelvis and beyond the rectus muscle which is felt to the medial side of a triangle, the base of which is formed by the pubic bone and the lateral sides by Poupart's ligament and the internal oblique and transversalis muscles attached to Poupart's ligament. If there is no sac present descending from the abdominal ring it must be obvious that constructing a new canal for the cord whatever the method employed, will have very little bearing on the closure of this defect.

Deficient Structures at the Pubic End of Canal—Dissection of the tissues involved will show that the conjoined tendon is absent and that the internal oblique and transversalis muscles pass over directly to the rectus sheath, leaving a defect which is often as much as one and one-half inches from the lower border of the muscle to the pubic bone and Poupart's ligament. In addition the fibers of the internal oblique muscle at the lower border are attenuated and weak. The greatest defect is at the border of the rectus and from there it extends lateralward with a diminishing width often as far as the abdominal ring. In this way the floor of the canal is often weak throughout its extent.

Attempts to close this defect by the ordinary methods of suture are not uniformly successful. Sutures in vogue affect only adhesions if successful but there is a distinct gap, and efforts to close this require that the suture be applied under tension. This is a violation of the cardinal principles of surgery. The sutures either cut out or absorb and the gap recurs. Neither can the fascia of the external oblique be overlapped here because the pillars of the ring at this point are fixed by their insertion into the pubes. In addition to that, the base of the triangle that is formed by suturing the internal flat muscles to Poupart's ligament is the pubic bone to which nothing is attached, consequently the angle cannot be completely obliterated.

Normal Structures at Pubic End of Canal—Normally the opening of the subcutaneous ring is protected by the conjoined tendon, which is inserted into the crest of the pubes and along the pectineal line behind the attachment of Gimbernat's or the lacunar ligament for the distance of about 1.25 cm. The pectineal line is covered by a strong band of fascia called Cooper's ligament, which extends lateralward from the pubic tubercle and merges

with the pectineal fascia. It is to this that Gimbernat's ligament and the conjoined tendon are attached.

The transversalis fascia in Hesselbach's triangle, especially in cases of direct hernia, is thin and attenuated and can offer very little resistance unless supported by other tissues. The principal support is derived from the conjoined tendon.

Essentials of the Proposed Operation—Before proceeding to describe the operation, it would be well to direct attention to two elements that are essential parts of the operation about to be described, namely, fascial suture and the fascial or ligamentous covering of the superior surface of the pubic bone.

The opening of the superficial inguinal ring is situated anteriorly, and immediately over the insertion of the conjoined tendon. Absence or attenuation of the conjoined tendon consequently creates a definite weakness at this point and is undoubtedly the cause of most instances of direct hernia.

The Use of the Fascial Suture—The use of fascia in operations for hernia was first reported by L. L. McArthur,¹⁹ in 1901, who published a second article²⁰ on the subject, in 1904. His method was employed in conjunction with the Bassini operation. In it he made use of strips of fascia derived from the aponeurosis of the external oblique. He states that other methods of suture are dependent for success upon the formation of cicatricial tissue between the opposing surfaces, and that we must expect occasional failure because of this very yielding cicatricial tissue, but that he had been able to demonstrate that his autoplasmic suture heals in situ, is not absorbed and does not slough. He presented microscopic specimens in verification of his statements.

Gallie and Le Mesurier,^{12, 13} in 1921 and 1923, called attention to the advantages of fascial suture. They proved beyond any doubt that fascia continues to live in an unchanged form after being used as suture material. It is, therefore, to be regarded as a transplant and not merely as a suture. In their cases the fascia was derived from the thigh, and they advised that it be woven over the defect. Case 12, upon whom an autopsy was performed, 57 days postoperative, illustrates the permanence of the fascial suture. Microscopic examination demonstrated that the histologic character of the fascial transplant had remained unchanged and that it was firmly anchored in the tissues through which it passed (Figs. 1, 2 and 3).

It is somewhat difficult to understand why the definite advantage resulting from the employment of fascia in the cure of hernia has not been more generally adopted. At about the time that McArthur presented his operation and advocated the use of fascial strips, there began to appear on the market various types of suture material, plain and chromic catgut, kangaroo tendon, silk, etc., that were put up and sterilized in glass containers. As they were ready for immediate use, and were easily obtainable and convenient, they came into general use for hernia as well as for other types of surgery.

There is, however, an essential difference between fascia and all other

PHOTOMICROGRAPHS OF THE FASCIAL SUTURE REMOVED FROM CASE 12 WHO DIED 57 DAYS POSTOPERATIVE, FROM THROMBOSIS OF THE LEFT COMMON ILLIAC ARTERY AND VENA CAVA

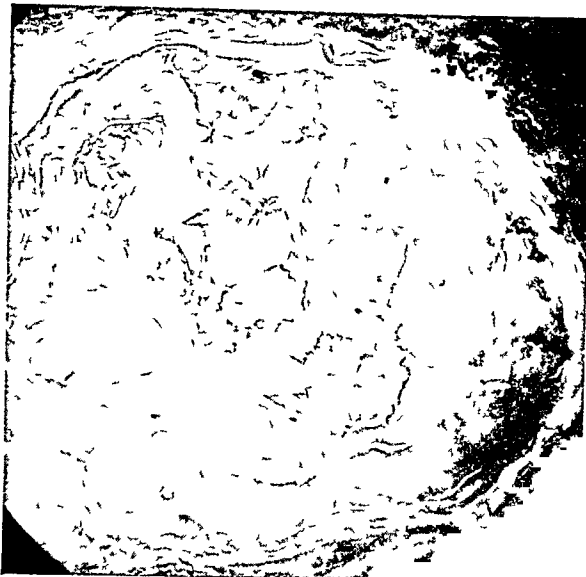


FIG 1.—Photomicrograph showing cross section of the fascial suture. The clear irregular areas in the center are artifacts, due to tearing of the tissues in sectioning. The clear area surrounding the fascial suture is also an artifact, due either to pulling on the suture before it was imbedded or to an uneven shrinking of the tissues in the fixing solution. The denser character of the fascial suture can be made out even at this magnification. At the upper left of the suture is adipose tissue. At the lower left are a group of blood vessels in the connective tissue surrounding the suture. (Low power)

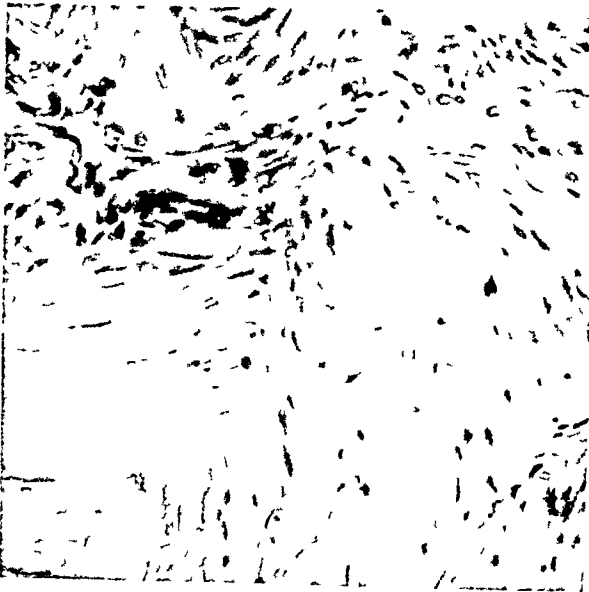


FIG 2.—Photomicrograph of area shown in Figure 1. On the left can be seen the dense compact fibrous structure of the fascial suture. A few scattered nuclei attest the viability of the tissue. To the right is the looser connective tissue through which the suture passes. The large pale vesicular nuclei indicate young growing fibroblasts. In the upper center is a small blood vessel and just below this, what appears to be new forming capillaries. (High power)



FIG 3.—Photomicrograph of an area on the edge of the fascial suture. This shows the many new capillaries forming in the areolar tissue at the edge of the suture. Blood cells can be seen in both of these. (High power)

sutures Fascia is a living transplant which remains permanently where it is placed, while all other forms of suture are eventually absorbed or cut out, and the strength of the wound is dependent upon the union that takes place while absorption is going on This difference appears to have been overlooked by the profession

The difficulties of securing fascia from the thigh as advocated by Gallie and Le Mesurier, and the complicated weaving necessitated, together with the additional time consumed, have been a bar to the employment of their method But the fact that recurrence of herniae during the war was so great as to disqualify enlistment of men who either had hernia or had been operated upon for it called attention forcibly to the necessity of devising some procedure that would make the cure of hernia more permanent

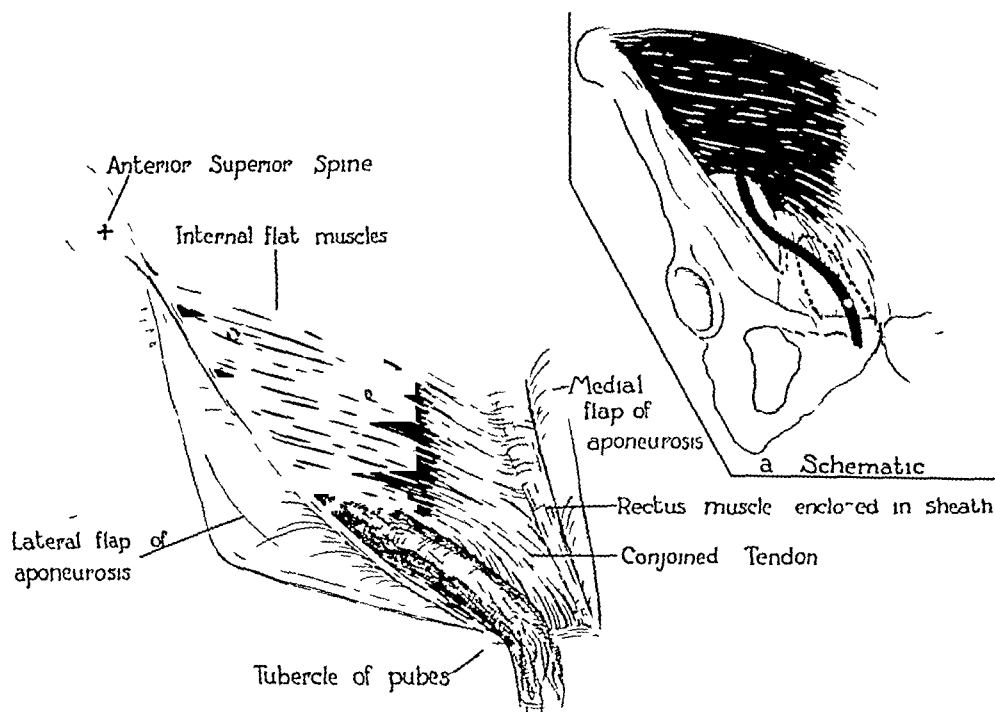


FIG 4—Normal deep layer of muscles (Redrawn from C. J. May, "The Normal Anatomy of the Inguinal Region") The deep flat muscles have their origin from the internal half of the anterior superior spine and lie anterior to the abdominal ring That portion forming the conjoined tendon is inserted behind the cord and the external inguinal ring, the location of which is indicated by the dotted line

Referring to the fascial covering of the pubic bone, the first suggestion as to its employment in operating for the radical cure of hernia, as far as can be ascertained, was made by W Wayne Babcock,⁴ in 1927 The fascia covering the superior surface of the pubic bone is several millimeters thick, and is composed of extensions on to the bone of Poupart's, Gimbernat's, Cooper's and the superior ligament of the symphysis It is tough, firmly fixed to the bone and is, therefore, admirably adapted for suture It is of particular value because the bone at this point forms the base of the triangle, already referred to, that cannot be successfully obliterated in any other manner except by direct suture to the bone at this point The operation described by Babcock was an ingenious one and was performed with a single suture of chromic catgut It was because of a recurrence following this operation in which chromic cat-

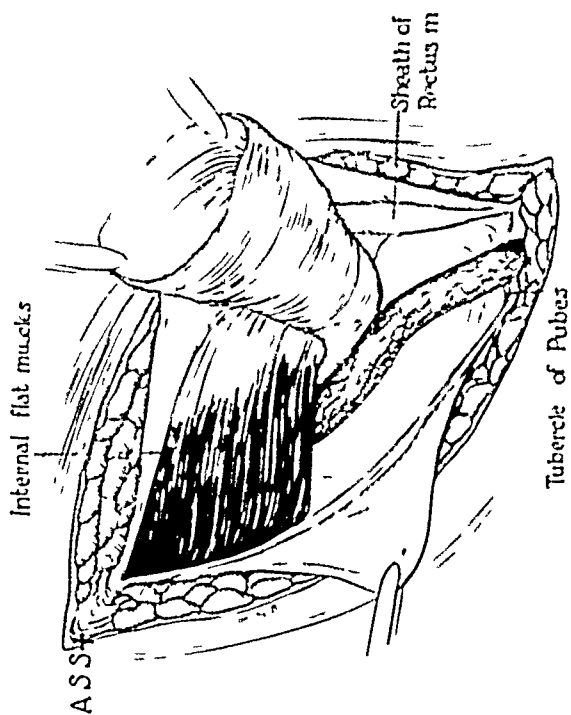
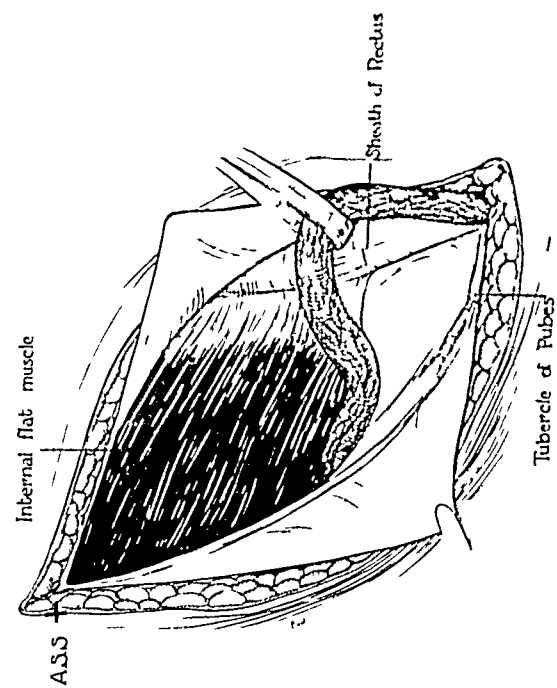


FIG. 6.—The defect on the lower border of the flat muscle makes a weak bed for the inguinal canal which undoubtedly favors the development of indirect hernia and favors recurrence of indirect hernia after operation as well as being the cause of direct hernia. In this case there were both an indirect hernia and a direct hernia. (Drawn from operated case by actual measurement.)



(Drawn from operated case by actual measurement.)
FIG. 5.—In direct hernia the lower fibers of the flat muscles are deficient so that, as a rule, there is no conjoined tendon, and the fibers of the muscle pass directly over the lower border

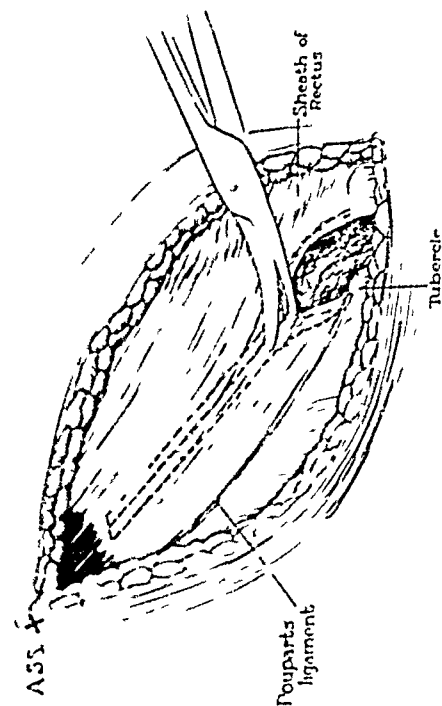


FIG. 8.—Outline, the fascial sutures. Incisions should all commence at the tubercle in order to insure firm attachment

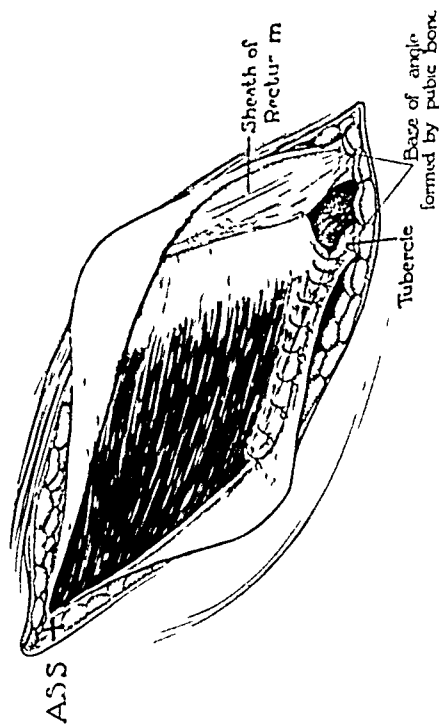


FIG. 7.—Angle that remains when tissues are sutured from side to side. Note that the bone which forms the base of the angle is not sutured. (Drawn from operated case by actual measurement.)

gut was employed, that I was led to investigate, more completely, the subject of the radical cure of hernia

It was to overcome the various weaknesses that appeared to have been present in other operations that the operation herewith described was devised. Free use has been made of the studies, investigations and work of others, which is hereby acknowledged

Operative Technique — (1) The incision is made down to the aponeurosis of the external oblique and in the direction of its fibers from a point sufficiently high to expose the belly of this muscle and extending down over the pubes sufficiently low to permit adequate exposure of the structures about the external ring. The flaps are carried back on either side to give wide and clean exposure of the aponeurosis

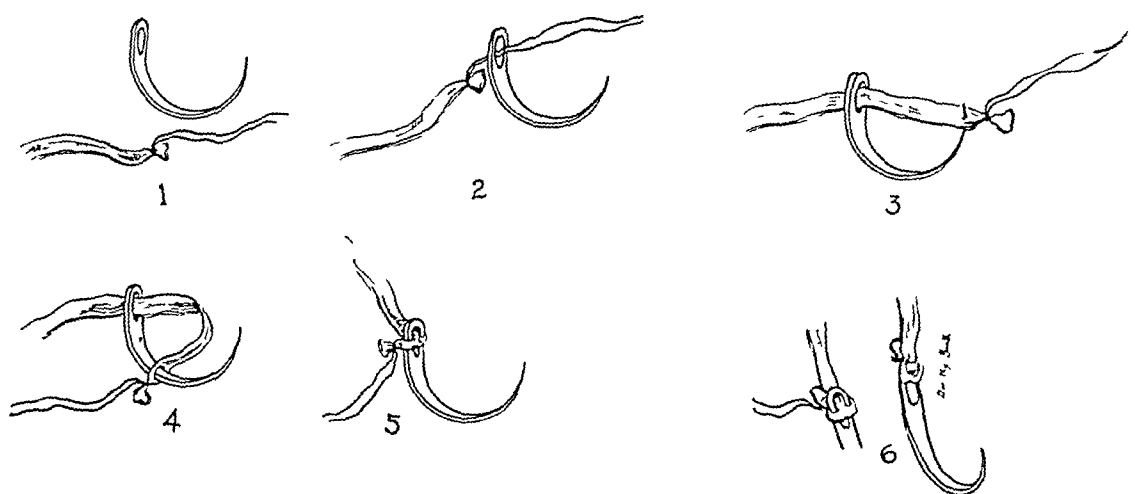


FIG 9 —Illustrating the method of threading the fascial suture on the needle

(2) The external spermatic fascia is dissected from the borders of the external ring and the pillars, and their origin exposed and isolated well down over the pubic bone, care being taken to free them of connective tissue. The canal is then opened by incising the aponeurosis from a point at the center of the apex of the external ring to the belly of the muscle, care being taken to follow the fibers of the aponeurosis and not to cut across them. This is accomplished with a pair of scissors which are only partly opened and are pushed along without a cutting motion. The two flaps of the aponeurosis are then separated from the underlying structures, both lateral- and medialward, exposing Poupart's ligament, particularly around the pubic tubercle to which it is attached, and then the internal oblique well beyond the border of the sheath of the rectus and down over the pubes

(3) The cord should then be carefully examined for any evidence of a sac of an indirect hernia. This is not infrequently found and if present it should be isolated, the neck twisted, ligated, and removed. The cord is then freed in its lower portion and the area of the direct hernia explored. As a rule the protrusion of the sac has disappeared unless it happens to be a very large one. I have never found that any good was accomplished by resecting these tissues in the presence of ordinary relaxation. If the sac is large it is,

of course, resected. It will usually be found that there is a wide space between the lower border of the internal flat muscles and Poupart's ligament and the pubic bone, and that the conjoined tendon is either absent or else very attenuated.

(4) In securing the fascial sutures, certain points are necessary in order to avoid unfortunate accidents. If the width of the strip is measured at the belly it will be found, when the pubic end is reached, that the strip may have been entirely severed by passing into the ring itself or have only a few inade-

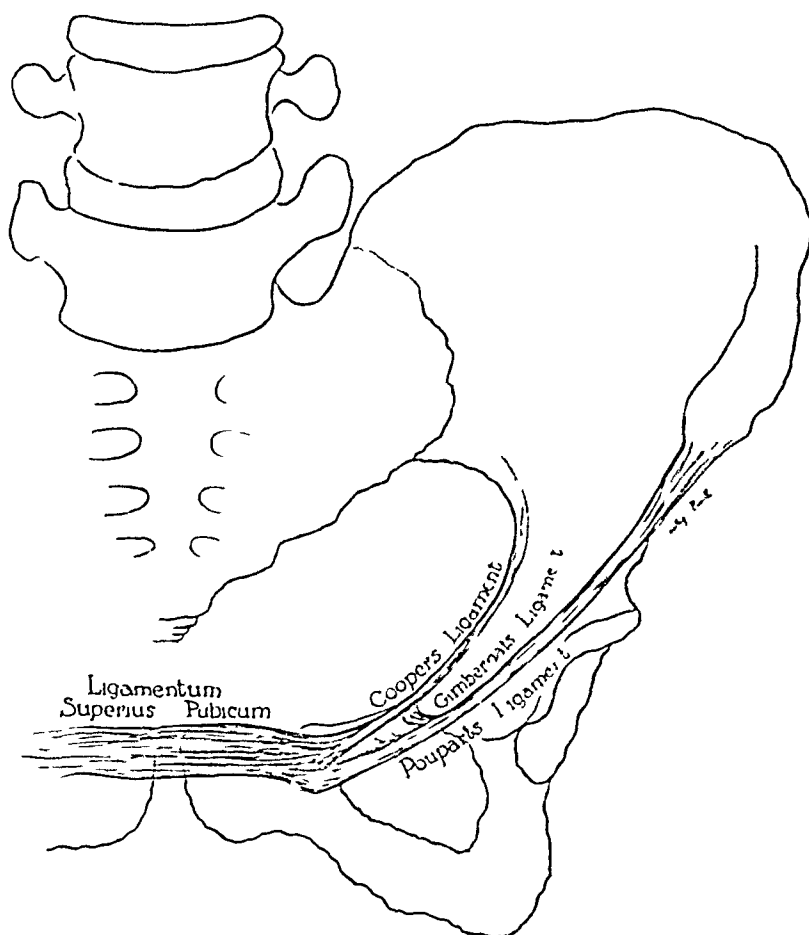


FIG. 10.—The thick, tough layer of fascia firmly attached to the superior surface of the pubic bone which appears to be extensions on to the bone of Poupart's, Gimbernat's, Cooper's and the superior pubic ligaments.

quate fibers remaining. As the firm attachment of the strip to the pubis is of prime necessity, the isolation of the strip should commence at the pubic end. After the initial incision, scissors may well be employed for completing the strip as already described. The medial strip is made first.

The next problem is threading the strip on the fascia carrying needle. If it is simply passed through the eye of the needle and then folded over and tied to the strip behind the eye, it will frequently slip out. The best method is to first tie the end securely to prevent its splitting, leaving the ends of the tie long enough to thread through the eye of the needle easily, bringing the end of the strip through from the posterior surface for a sufficient distance, so

that the point of the needle can pierce the end of the strip behind the ligature. The pierced end of the strip is then slipped back over the eye of the needle, which makes a friction knot that holds securely and uses up very little of the fascia.

The fixation of the end of the suture is important. Operators who have used fascial sutures have various ways of fixing the terminal knot. I do not use the knot for two reasons. One is that the knot uses up fascia unnecessarily which at best is not too abundant. The other is that the simple method of fixing the end to underlying fascia or to the suture itself by suture is better. This is best effected with fine silk. The stitch commences with a bite in the underlying fascia or suture and comes up through the edge of the suture and is carried back on the other edge in the same manner, after which it is tied. Two of these sutures are used.

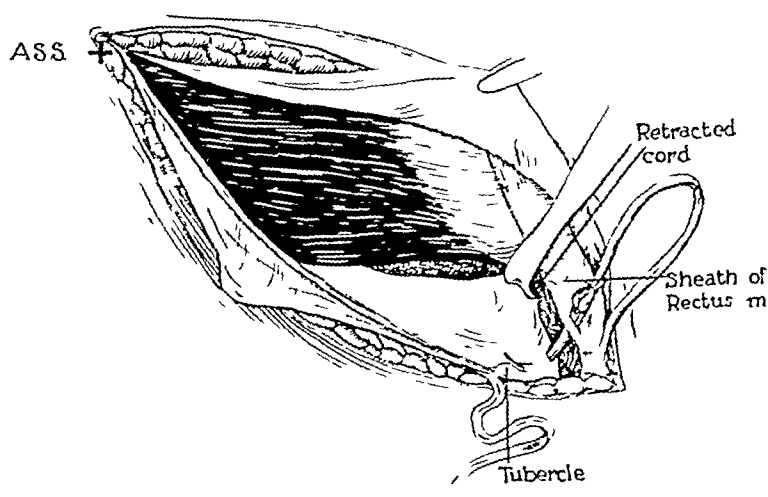


FIG 11—Tissues to be sutured, showing first stitch being introduced. This fascial suture is derived from the medial pillar and is carried through the rectus sheath and muscle and then passes over the cord, and takes a firm bite in the fascia covering the pubic bone.

(5) The cord is then held back medialward under the rectus by a small retractor and the suture is passed through the rectus sheath and the muscle and over the cord and then takes a good bite in the fascia that covers the pubic bone at the pecten ossis pubis.

This last point is to be selected so that the suture may not unduly compress the cord and at the same time fit it very snugly. This forms a new ring for the cord that is strong and unyielding, because the fascia passes over the cord in the direction of its fibers. It is not like the normal external ring, in which the application of force separates the fibers. The fascial stitch is then continued, passing through the rectus in the same manner and is sutured to the pubic bone. As a rule only two stitches include the rectus and the pubic bone, the last being passed at a point near the tubercle. After that the suture embraces the thick part of the internal flat muscles together with the transversalis fascia and Poupart's ligament. In passing the fascial suture it must be borne in mind that it is not a suture for approximating

surfaces but is transplanted tissue, and that the object is to secure good anchorage, therefore, the thicker the tissue through which it passes, the better. When Poupart's ligament is reached the first stitch should embrace Gimbernat's ligament, after which it is continued on Poupart's ligament until the point of origin of the internal flat muscles is reached. It is usually

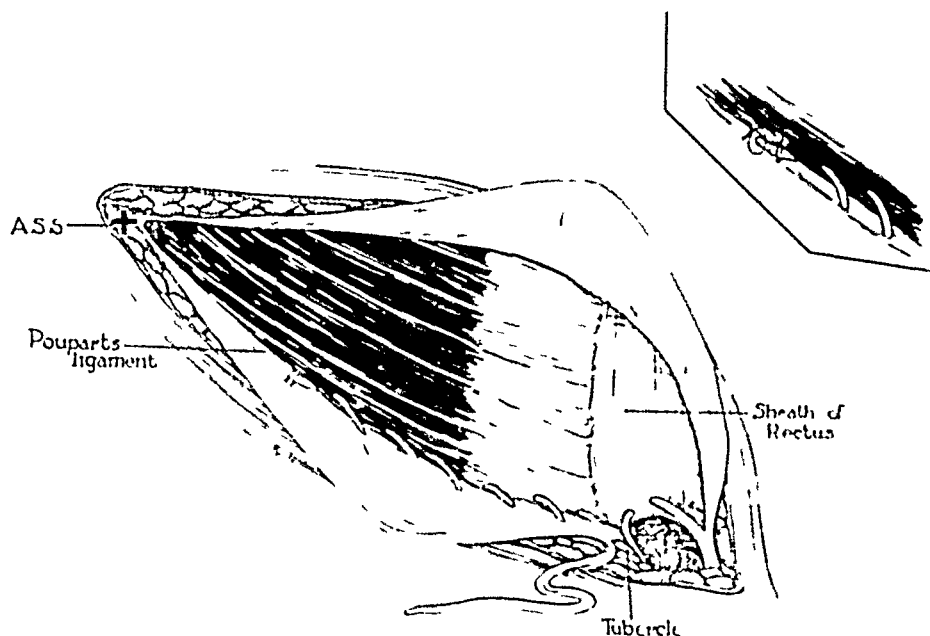


FIG. 12—The first suture line completed. The suture passes over the cord and forms a firm ring. Care must be taken not to compress the cord unduly.

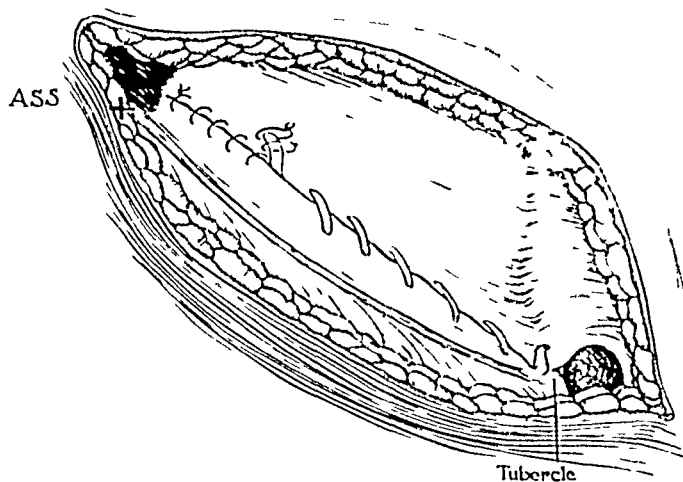


FIG. 13—Second suture line completed. The suture passes from the pubic tubercle to which it is firmly attached to the opposite leaf of the fascia making a new and undilatable external ring.

long enough for this purpose. If not, one or two stitches of chromic catgut may be employed to complete the line of suture. As there is little if any tension at this point, chromic catgut is sufficient.

(6) The second fascial suture is derived from the lateral pillar. After being prepared and fixed to the needle it is employed to close the interval left in the aponeurosis after the removal of the strips. The stitch is first

passed just over the emergence of the cord to the opposite edge of the aponeurosis and continued until the gap is closed. If not sufficient for this, the suture line may be concluded with chromic catgut, as there is no tension here and the suture line is immediately over the thick belly of the internal flat muscles.

It will be observed that by passing this last suture across to the opposite leaf of the aponeurosis, just above the cord, this point, which is normally the weak point, is further strengthened, because the fascia extends across in the direction of its fibers and makes a strong closure, whereas, if the fibers of the aponeurosis are simply sutured together, bringing their lateral aspects in juxtaposition, it is much easier for the fibers to be separated by continual pressure from above.

COMMENT

Normally there is no muscle behind the cord except the conjoined tendon, and the canal is closed by the shutter action described. When there is a defect in the muscle impairing this action, it is necessary to carry the fascial suture up to close this defect. By taking a deep bite through the thick part of the muscle, the fascial strip comes into contact with the perimysium of the muscle and is firmly anchored. In addition, the suture acts as a tendinous attachment to the structures to which the muscle is sutured.

It is a mistake to employ only one procedure for all herniae. The operation should be predicated upon the existing pathology.

The surgical rules that apply to suturing under tension do not apply to the fascial suture. It does not cut out or absorb but becomes a permanent transplant.

When a sac of an indirect hernia is present it is removed by high ligation and covering the stump over by a purse string suture of the transversalis fascia. This opening lies behind the origin of the flat internal muscles which amply protect it.

The advantage of separating the various layers in the abdominal wall is not only to facilitate the operation but also to permit them to fall into a new relationship after the suture is completed, thereby affording additional support.

The fascia is resistant to infection. Where infection has occurred in dealing with very large herniae, especially when incarcerated, the fascia is not involved. I have seen the glistening fascia where it was exposed and it has remained viable and effective.

The operation described protects the external ring even more effectively than the normal insertion of the conjoined tendon does.

Every case of hernia should be examined for weakness at the pubic end and whenever found the defect should be closed as described, irrespective of what may have been done in order to repair any coexisting hernia.

The cord is allowed to remain without disturbing its attachments more than is necessary to remove the sac, should one be present.

When for any reason the fascia from the pillars of the ring is inadequate, fascia can be secured from the fascia lata in abundance by using the Masson¹⁸ stripper.

The chief defect in earlier operations for inguinal hernia, as far as direct hernia is concerned, was in the attempt to close the angular defect by suture from side-to-side, which cannot be accomplished satisfactorily.

The introduction of the autogenous fascial suture has markedly improved results in the operation for inguinal hernia as a whole, as the results obtained by the Mayo Clinic, Seelig²⁰ and Payne²¹ show. Still, it does not appear that the fascial suture has been as generally adopted as its value would seem to warrant. The high percentage of recurrences following operations for direct hernia has been an embarrassment to surgeons, which I believe the employment of the procedure herewith suggested will obviate. We must get away from viewing the sac as the exclusive cause of hernia and direct attention to the anatomic defect at the pubic end of the canal, which not only is the cause of direct hernia, but is, I believe, a contributing factor in the development of indirect hernia.

The operation herewith presented can be almost as easily and quickly performed as those in which prepared sutures are employed. The only additional time that is required is for the preparation and threading of the fascial sutures.

CASE REPORTS

Case 1—No. 39-159. June 21, 1934. Male, age 61, farmer.

Duration—First noticed in 1917. Operated in 1925. Recurrence several weeks ago.

Physical examination—Right direct inguinal hernia.

Operative findings—Round aperture lying on pubic bone with irregular sac.

Operative procedure—Sac isolated, ligated and excised. Operation completed as described.

Result—April, 1938. Doctor reports no evidence of hernia.

Case 2—No. 40-15. January 21, 1935. Male, age 27, laborer.

Duration—Five years.

Physical examination—Double hernia. On both sides, on invagination of scrotum, finger passes directly over pubic bone into pelvic cavity. On right side hernia comes down into scrotum.

Operative findings—Indirect sac on both sides.

Operative procedure—Sac isolated, ligated and excised, and reinforced by suturing transversalis fascia over neck. Operation completed as described.

Results—April, 1938. Doctor reports no evidence of hernia.

Case 3—No. 40-32. January 24, 1935. Male, age 19, clerk.

Duration—Two years.

Physical examination—Left inguinal hernia. Does not enter scrotum. On examination, finger passes over pubic bone into abdomen. Can palpate edge of rectus.

Operative findings—No sac in relation to cord, lower segment internal flat muscles and conjoined tendon deficient. Fibers of muscle pass directly to rectus sheath.

Operative procedure—Operation completed as described.

Results—Has moved out of the state but reported over phone. "Has no trouble, perfect result." Since above note, patient returned to city for examination. No evidence of hernia was found.

Case 4—No. 40-52. February 21, 1935. Male, age 48, bank official.

Duration—First noticed 21 years ago.

DIRECT INGUINAL HERNIA

Physical examination—Both external rings enlarged and has protrusion at external rings On invagination of scrotum, on both sides, finger passes over pubic bone directly into abdominal cavity

Operative findings—Deficiency of lower segment of internal flat muscles and conjoined tendon on both sides

Operative procedure—Operation on both sides completed as described

Result—April, 1938 Examined by myself No evidence of hernia

Case 5—No 40-64 March 8, 1935 Male, age 36, farmer

Physical examination—Both inguinal rings open and admit end of finger when scrotum is invaginated Diagnosis Chronic appendicitis, double hernia

Operative findings—No sac Muscle deficiency

Operative procedure—Appendix removed through muscle-splitting incision Operation on both sides completed as described

Result—April, 1938 Doctor reports no evidence of hernia Since above note, patient returned to city for examination No evidence of hernia found

Case 6—No 40-89 March 27, 1935 Male, age 61, farmer and laborer

Duration—Five months

Physical examination—Right inguinal hernia, easily reducible, increasing in size Has never extended into scrotum No pain No obstruction

Operative findings—Deficiency of muscle and conjoined tendon Large defect Mouth of sac extended nearly entire length of inguinal canal

Operative procedure—Isolation of sac, ligation, excision Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 7—No 40-97 April 2, 1935 Male, age 44, traveling agent

Duration—One and one-half years

Physical examination—Undescended testicle on right side On standing has a large hernia which does not extend to scrotum Reduces easily Marked defect in external ring On invagination of scrotum, pubic bone is easily palpated and finger passes into abdominal cavity

Operative findings—Large defect at lower margin of internal flat muscle, no conjoined tendon Testicle in separate sac Chronic appendicitis, adherent to neck of sac

Operative procedure—Appendix removed through muscle-splitting incision, sac isolated, removed, neck sutured over with fascia transversalis Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 8—No 40-138 May 9, 1935 Male, age 33, laborer

Duration—Fourteen or 15 years

Physical examination—Left inguinal hernia well down in scrotum Difficult to reduce Pubic bone easily palpated External ring small

Operative findings—Lower segment of internal flat-muscles deficient and conjoined tendon consists of only a few fibers Sac led up to internal ring

Operative procedure—Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia Patient developed hernia on opposite side

Case 9—No 40-158 May 21, 1935 Female, age 59, secretary

Duration—Twenty years

Physical examination—Truss discarded four years ago because ineffective Hernia easily reduced Pubic bone easily palpated

Operative findings—Conjoined tendon lacking Hernia is fatty type with small sac originating at abdominal ring

Operative procedure—Sac isolated, ligated and removed Operation completed as described

Result—April 22, 1938 Examined by myself, no evidence of hernia

Case 10—No 40-274 October 19, 1935 Male, age 59, superintendent of coal mine

Duration—One year

Physical examination—Left inguinal hernia Does not enter scrotum Large subcutaneous ring Pubic bone easily palpated Protrusion appears on standing Disappears on lying down

Operative findings—Hernia came through immediately under subcutaneous ring Only slight contact with cord Entire absence of conjoined tendon

Operative procedure—Operation completed as described

Result—April, 1938 Examined by myself, no evidence of hernia

Case 11—No 40-325 December 30, 1935 Male, age 34 truck driver Hits heavy boxes containing metal

Duration—Many years

Physical examination—Right inguinal hernia Massive incarceration extending one third distance down thigh

Operative findings—Two segments of intestine, one obstructed Reduced through right rectus incision Conjoined tendon poorly developed Sac isolated and neck sutured

Operative procedure—Operation completed as described

Result—April 21, 1938 Examined by myself, no evidence of hernia

Case 12—No 41-26 January 25, 1936 Male, age 60, farmer and cannery

Duration—Seven years

Physical examination—Left inguinal hernia Massive incarceration Syphilitic, paralyzed on right side, speech affected

Operative findings—Incarcerated sliding hernia containing sigmoid with hypertrophied appendices epiploicae and mesosigmoid Cord pushed down in front of sac Enormous aperture one and one-half inches in diameter

Operative procedure—Sac incised below mesosigmoid sutured and returned Operation completed as described

Subsequent Course—Two weeks following operation developed a thrombosis of common iliac arteries and veins affecting both legs Death from gangrene 57 days post operative Autopsy demonstrated thrombi Site of hernia excised for study Hernia canal found obliterated Pathologic examination of the fascial suture demonstrated that the histology was unaltered

Case 13—No 41-61 February 29 1936 Male, age 56, machinist

Duration—Some years

Physical examination—Right inguinal hernia Indirect sac On invagination of scrotum, finger passes directly over pubes into the abdominal cavity

Operative findings—Well-defined oblique sac Conjoined tendon practically absent

Operative procedure—Sac isolated, ligated and excised Operation completed as described

Result—April, 1938 Examined by myself, no evidence of hernia

Case 14—No 41-77 March 26, 1936 Male, age 37, farmer and rural mail carrier

Duration—Eight years

Physical examination—Left inguinal hernia, incomplete Hernia comes down in canal on coughing but is not complete On invagination of scrotum, finger passes over pubic bone to its posterior surface

Operative findings—Sac of hernia had a very broad base alongside the cord, showing deficiency of posterior wall of canal Conjoined tendon very poorly developed

Operative procedure—Sac isolated, excised and closed by suture Operation completed as described

Result—Doctor reports no evidence of hernia

Case 15—No 41-120 May 30, 1936 Male, age 20, laborer, works on roads

Duration—Four weeks

Physical examination—Right inguinal hernia History of knot size of hen's egg, appearing while at work On invagination of scrotum, finger passes over the pubic bone

DIRECT INGUINAL HERNIA

Operative findings—No sac found Conjoined tendon and lower segment of internal flat muscles absent

Operative procedure—Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 16—No 41-131 June 3, 1936 Male, age 32, laborer

Duration—Six years

Physical examination—Right inguinal hernia Truss ineffective On invagination of scrotum, finger passes directly over the pubic bone

Operative findings—Congenital sac extending along cord Central portion obliterated, below the sac is continuous with the tunica vaginalis Conjoined tendon entirely absent, muscle fibers passing over directly to rectus sheath, external ring large

Operative procedure—Sac isolated, ligated and excised Lower portion of sac isolated and constructed into a tunica Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 17—No 41-171 July 25, 1936 Male, age six

Duration—From birth

Physical examination—Right inguinal hernia extending into scrotum Easily reduced On invaginating scrotum, finger passes directly over pubic bone and into abdominal cavity

Operative findings—Definite sac extending to testicle No abdominal ring Neck of sac included whole of posterior wall of canal Lower segment of internal flat muscles and conjoined tendon absent

Operative procedure—Sac removed Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 18—No 41-193 August 22, 1936 Male, age 65, dairyman

Duration—Four years Four months ago hernia began to slip under truss

Physical examination—Right inguinal hernia On invaginating scrotum, finger passes over pubic bone directly in for some distance

Operative findings—Cord had a sac running along it but contained no intestine Lower segment of internal flat muscles and conjoined tendon lacking, producing a large defect behind external ring

Operative procedure—Sac isolated, ligated and excised Operation completed as described

Result—April, 1938 Examined by myself, no evidence of hernia

Case 19—No 41-284 November 28, 1936 Male, age 46, laborer and farmer

Duration—Some years

Physical examination—Double hernia Right inguinal hernia, direct Left inguinal hernia Femoral hernia on right side and spermatocele on left On invaginating scrotum, on both sides finger passes over pubic bone directly into abdominal cavity

Operative findings—No sac found on right, muscle deficiency On left side, no conjoined tendon, muscle deficiency Left aperture $2\frac{1}{2}$ cm

Operative procedure—On right side, rectus sheath and muscle sutured to Cooper's ligament, behind femoral hernia, protecting both femoral and direct hernia Operation completed as described on left side only

Result—April, 1938 Doctor reports no evidence of hernia

Case 20—No 42-77 April 14, 1937 Male, age 48, captain in fire department

Duration—Two years

Physical examination—Right inguinal hernia Protrusion extends half way to scrotum when standing Cannot wear truss Reduces when he lies down Hernia is large On invagination of scrotum, finger passes over pubic bone into abdominal cavity

Operative findings—Definite sac extending several inches along the cord Conjoined tendon present but very attenuated

Operative procedure—Sac isolated, ligated and removed Operation completed as described

Result—April, 1938 Doctor reports no evidence of hernia

Case 21—No 42-86 April 16, 1937 Male age 26, ambulance attendant

Duration—One month

Physical examination—Left inguinal hernia Sudden onset of pain in left inguinal region while carrying patient downstairs on a stretcher Protrusion occurred later Has protrusion when standing, reduces when lying down On invaginating scrotum, finger passes inward directly over pubic bone Also has varicocele and elongated scrotum

Operative findings—Small sac at midpoint of Poupart's ligament No conjoined tendon and muscle fibers pass directly to rectus sheath at a point about 5 cm above crest of pubes

Operative procedure—Sac isolated and removed Operation completed as described Resection of pampiniform plexus, amputation of scrotum

Result—April, 1938 Examined by myself, no evidence of hernia

Case 22—No 42-96 April 22, 1937 Male, age 28, sheet metal works

Duration—Five years Second recurrence three months ago First recurrence one month after operation Second recurrence one and one-half months after operation

Physical examination—Direct hernia, left

Operative findings—Dissection showed only aperture was just above pubic bone, where the opening easily admitted the finger

Operative procedure—Scar tissue cut out Issues dissected out and demonstrated Aperture closed by suturing rectus muscle and sheath to pectin ossis pubic with strip fascia from fascia lata

Result—April 30, 1938 Examined by myself, no evidence of hernia

Case 23—No 42-245 November 11, 1937 Male age 61, minister

Duration—Recent occurrence

Physical examination—On standing, has protrusion at external ring on left side, which reduces when he lies down On invagination of scrotum finger passes in directly over pubic bone

Operative findings—Long slender sac between pampiniform plexus and cord down to external ring Accompanying the sac was a globular pad of fat Finger passes directly through external ring to inside of pelvis

Operative procedure—Sac isolated, ligated and excised Operation completed as described

Result—April, 1938 Examined by myself, no evidence of hernia

Discussion—The series in which the technic described in this paper was applied consisted of 23 patients, among whom there were four who had double herniae, making a total of 27 operations This number of operations, while not large, were all performed by myself in an attempt to find out why herniae recur In each case the tissues were thoroughly isolated by dissection and their insertion exposed, and the facts revealed studied in the light of what had been written on the subject

The key to the diagnosis of direct hernia was the maneuver of invaginating the scrotum and passing the finger over the plainly felt superior surface of the pubic bone into the cavity of the pelvis beyond the insertion of the rectus muscle The defect thus demonstrated was more marked in some cases than in others but was, however, definite in every case In some of the cases two fingers could be introduced and swept around beyond the insertion of the rectus muscle

I was able to demonstrate, in every case, that where this maneuver indicated that the conjoined tendon was deficient, on dissection it was found

to be absent. In addition to that, it was found that the lower bundles of fibers of the internal flat muscles were also absent. The widest gap above the pubic bone was 5 cm (two inches), but the defect was not confined to the region of the external ring but extended lateralward to the internal ring or beyond. This probably explains why there are recurrences following operations for indirect hernia. It is now generally conceded that recurrence in these cases takes place below the internal ring.

The lower segment of the internal flat muscles and the conjoined tendon, which is a continuation of them, produce the shutter action referred to by Sir Arthur Keith,¹⁷ so that there is not only a defect but a lack of this very important shutter action. I was able to demonstrate this very clearly in a case of indirect hernia with a rather large external ring but with an intact conjoined tendon. When the little finger was introduced into the inguinal canal and the patient coughed, the finger was constricted very firmly by the muscle.

In each case, notwithstanding the fact that the hernia was a definite direct one, the cord was examined carefully for a sac. In 14 of the 27 herniae a sac was found. Some were rudimentary, others larger. An interesting condition was found in three cases where the mouth of the sac was very large, corresponding to the length of the posterior wall of the inguinal canal.

Follow-Up—All of the cases have been reexamined, either by the patient's attending physician or by myself, during the month of April, 1938. In every case the findings were the same. On invagination of the scrotum, the external ring was found to be firmly closed, so that not even the tip of the finger could be introduced. There was no bulging or protrusion at any point while standing, coughing or straining.

Congenital Condition—From the uniformity with which the deficiency in the lower segment of the internal flat muscles and the absence of the conjoined tendon were found, it may be reasonably inferred that the predisposing cause for direct inguinal hernia is the presence of a congenital condition. This was borne out in this series of cases by the occurrence in three cases, whose ages were six, 19 and 20, respectively, in which it was noted that the lower segment of the internal flat muscles and the conjoined tendon were deficient. In the 19 and 20 year old cases, there was no sac. In the six year old case, there was a peculiar sac, in that there was no internal abdominal ring and the mouth of the sac included the whole of the posterior wall of the inguinal canal.

CONCLUSIONS

- (1) Direct inguinal hernia is caused by a deficiency of the lower segment of the internal flat muscle and the conjoined tendon.
- (2) This appears to be a congenital condition but as a rule the hernia does not appear until later in life.
- (3) The defect can be closed with certainty only by the use of fascial suture.

(4) This defect presents the shape of an irregular triangle in which the base is the pubic bone. In closing this defect, the rectus muscle and the sheath must be sutured first to the ligamentous tissue covering the superior surface of the pubic bone, after which the internal flat muscles are sutured to Poupart's ligament, thus completing the closure.

(5) The operations described by Bassini, Halsted and Ferguson visualize hernia as being a sac protruding through the inguinal canal, and the operations are directed toward removal of the sac and the construction of a new and stronger canal for the cord. Direct hernia has no relation to the canal and the cord except that it appears at the lower end. The problem of curing direct hernia by one of these standard operations suggested modifications that have not been successful.

(6) The examination for inguinal hernia should always include invagination of the scrotum and exploration of the external ring and the superior surface of the pubic bone. If the finger passes directly over the pubic bone into the pelvic cavity there is a defect which must be closed as described, irrespective of what else may be found necessary to be done for other conditions.

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DISCUSSION OF THE PAPERS OF DOCTORS ROBINS AND WILLIAMS

DR A O SINGLETON (Galveston, Texas) I wish to congratulate both essayists upon this excellent exposition of the repair of defects in the inguinal region I would like to direct my remarks to Doctor Robins' paper Doctor Robins has been thinking about these herniae for a long time, and has written upon the treatment of them previously We know that where we have marked strain on the abdominal wall it is usually well supplied with fascia As has been as well demonstrated, the great difficulty in repairing these defects is in the absence of fascia About 1917, I read a paper reporting eight cases of transplanting some fascia in cases of inguinal hernia, and have practiced it on very difficult herniae, both direct and indirect, at different times A few years ago the literature became filled with reports of fascial sutures, and I started employing these in place of fascial patches Doctor Robins' suggestion of using this fascia has recalled some unpleasant experiences I worked with these, trying to make and tie them, but it meant hours of work and not always satisfactory results, so I finally returned to the employment of the patches of fascia

I looked up all the cases we have had and found there had been 54 transplants of fascial patches, in very difficult inguinal herniae, direct and indirect, selecting the difficult ones, as a rule those that had recurred From the very first we practiced exposing the inguinal region, in preparation for repair, as one would by any other method Under local anesthesia, a patch of fascia was removed from the thigh, after measuring the approximate size of the opening which was to be filled A notch was cut in one end, and the cord placed through near the notch It was then sutured along the inguinal ligament with fine chromic catgut silk and sutured carefully to the pubic bone The fascia was then picked up with mattress stitches through the internal oblique muscle and these sutures were not tied at this time The hernia was then repaired in the usual way, the muscle being brought down under the cord after which the mattress stitches were tied Following this the external oblique was brought together as one would do ordinarily In other words, this transplant was placed behind the muscles and then a Bassini hernia operation was performed over it Out of 54 cases, selected from probably 1,200 herniae, extending over a period of some years, we have not been able to find one that has had a recurrence We have had the

wound infected and drained for several days but no grafts have been lost. This method has, therefore, been found to be efficient for the cure of these defects in the inguinal region, and has not been followed by a recurrence in a single case.

DR WILLARD BARTLETT (St. Louis, Mo.) I feel quite qualified to discuss this subject, I think, because of the fact that I have had more grief than anybody else with herniae. My outstanding result was on an old hospital orderly upon whom I operated for a bilateral recurrence after ten operations upon both sides for direct herniae. I am too modest to tell you what my result was, but he does not come in on the cases referred to above.

In this class of case, we adopted the following procedure for want of something better. We incised the skin, exposed the herniated mass, picked up the cord, pushed the herniated mass into the ring, and wove in fascia sutures like a chair bottom. We picked up the ring wherever we could get it, crisscrossed the sutures, and when completed, the individual could not push out his hernia at all. I do not remember a recurrence, though a number of cases are of long duration.

DR CHARLES R. ROBINS (closing) I should like to say a word about the reference made to me in Doctor Williams' paper. One could not help but be pleased to realize that an expedient I had practiced some years ago should lead to the development of a standard operation for the cure of indirect hernia. The case in which I first performed the operation for the relief of hernia through an abdominal incision was to relieve a strangulated femoral hernia, which had been incarcerated for some time, and there was a possibility that it might be necessary to resect the intestine.

I had previously reduced a strangulated femoral hernia by incising Gimbernat's ligament, a procedure which had long been advocated. However, in this case, although the reduction resulted in the recovery of the patient from the strangulation, she subsequently developed a very large femoral hernia that could not be repaired.

I found that by approaching the hernia from above, through an abdominal incision, the reduction was simplified, and that it afforded ample space in which to resect the intestine, if necessary. I have approached the hernia from the abdomen in strangulation in a number of cases but have not adopted the procedure for the cure of simple hernia as a routine procedure. Doctor LaRoque developed the operation as a curative procedure, and Doctor Williams has still further developed it. One also sees very favorable references to the procedure in the literature.

Referring to Doctor Singleton's remarks, I have used the patch fascial transplant in a few cases with satisfactory results. The fascial suture is, however, a more convenient and more easily applied method of using the fascia. My first observation of the use of the fascial suture was at the Mayo Clinic some few years ago. Doctor Masson had devised a stripper, which I have found a most satisfactory instrument. However, I have not found it necessary to secure fascia from the thigh except when the pillars of the rings could not be used. The objection to getting fascia from the thigh, either patch or a suture, is that it makes two operations, and consequently prolongs the procedure.

The operation that I have shown is a simple one and can be done as quickly as when the prepared sutures are used. The only additional time required is to prepare the fascial strips and to attach them to the needle. This, however, is a matter of only a few minutes.

MADELUNG'S DEFORMITY

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MADELUNG'S deformity may be described as an idiopathic, progressive curvature of the radius due to a dyschondroplasia of the inferior radial epiphysis, resulting in a deformity of the wrist, giving it the appearance of an anterior (or, more rarely, a posterior) subluxation of the hand. Several earlier authors, including Madelung himself, have accredited Dupuytren with the first reference to this condition, while others have given it the double patronym of "Dupuytren-Madelung," but Stetten,²²¹ who has carefully examined Dupuytren's right to this distinction, finds that it cannot be substantiated. Dupuytren's report,⁷³ in 1834, is based on a quotation taken, by his own admission, from Bégin,¹¹ who, in 1825, noted among adult male workers, not the typical spontaneous deformity, but a true forward dislocation of the wrist as a result of occupation. Other similar reports of a vague²¹³ or secondary static deformity¹³⁰ appeared soon after.

Probably the first description of the true deformity was that by Malgaigne,¹³⁸ in 1855, while in 1875 Jean¹¹⁵ reported the first definite anatomic dissection. But the credit for first presenting a clear picture of it as a distinct clinical entity reverts to Madelung,¹³⁵ who, in 1878, before the Seventh Congress of German Surgeons, described the condition as a disturbance of growth in the joints, analogous to pes valgus, genu varum and scoliosis, and regarded it as a subluxation of the wrist joint. It remained for Duplay,⁷¹ in 1885, to point out that the deformity was a result of volar bowing of the distal end of the radius.

Practically all that has been written on this subject has appeared in the French, German and Italian literature, and it was this fact, together with the paucity and meagerness of references to the subject in the various textbooks, that prompted Stetten,²²¹ in 1909, to describe, in American literature, a case of the deformity which he had previously reported²²⁰ abroad, and at the same time presented a complete review of the literature relating to it.

Although he definitely mentions several previously reported cases in America, he has been misrepresented by subsequent authors as having reported the first case from this country. At the present time one finds the reports of cases of this condition in a deplorable state. They are inadequate, often vague and unconvincing, while references are meager and all too frequently incorrect. Instead of being content with a case report, a quasi review of the

literature has been presented which merely serves to perpetuate the inaccuracies of previous writers

Pooley,¹⁷⁶ in 1880, evidently totally unaware of Madelung's report, described the first authentic case in American literature. Kieffer,¹²⁰ in 1902, briefly described another, Peckham,¹⁶⁵ in 1907 poorly presented a questionable case in a girl, age 14. Brinsmade,²⁸ in 1909, reported the fourth case, Stetten²²¹ wrote his incomparable article in 1909, a few months later Peckham and Hammond,¹⁶⁶ in a presentation of interesting cases from their clinic, reported two cases (Nos. 3 and 4) as examples of Madelung's deformity. In one of these no evidence or description warranting a definite diagnosis of the genuine deformity is given, although the other case (No. 3) is an excellent example of the rare reverse type of the deformity. Stokes²²¹ added two more American cases in 1910, while in 1911, Jones¹¹⁶ briefly described another case, and Taylor²²⁵ reported two cases in 1912. In 1914, Adler¹ briefly described a case which he called Madelung's deformity, while in 1915, Parkes¹⁶¹ reported a case upon which he had operated with excellent results. In 1916, Earl⁷¹ gave a good presentation of an early case of the deformity.

Despite the availability of these reports in American literature, or at least their mention in Stetten's article, Brown,¹¹ in 1924, reported his case as "the fourth case reported in America," while in the same year Levyn,¹³² realizing Brown's mistake, as he thought, wrote a "report of two cases constituting the fifth and sixth American cases," when in truth they were really the sixteenth and seventeenth. Also in 1924 Moore¹⁷⁴ reported two cases upon which he had operated, while in 1936, Claiborne¹¹ reported a case. Emboldened by a thorough, methodical and exact survey of the related American literature, we feel we are correct in reporting the case herein cited as the twenty-first from this country. Two reports¹⁶²⁻²⁷⁸ have not been included in this series since they obviously do not fall into the category of a true Madelung's deformity, presenting, as they both do, lesions of the ulna and not of the radius.

Comprehensive reviews on this subject have appeared from time to time. In 1903, Abadie¹ compiled a bibliography reporting 41 known cases of the deformity which he had succeeded in collecting. Gasne⁹⁵ reviewed the subject in 1906, but did not add any new cases. In 1907, Estoi⁷⁷ published a total of 85 cases. Stetten²²¹ collected, and gave brief summaries of 62 cases up to 1908. In 1908, Siegmist²¹² tabulated 58 cases, and Franke⁸⁷ only 56. In 1909, Maisan¹⁴⁰ listed 90 cases, in 1911, Ramos¹⁸⁵ listed 69 cases, while in 1913, Melchior,¹⁵² after reviewing the subject, accepted only 75 cases, while in 1933, Salisachs²⁰³ reported a total of 133 known cases.

The discrepancy in these figures is obvious, and is due to the considerable difference of individual opinion as to what constitutes a true instance of this deformity and on what evidence it is to be accepted. Although only five cases reported by Madelung are specific enough for acceptance, he claims to have seen 12, and he is sometimes credited with that number. In the discussion of Madelung's paper,¹³⁵ Czerny claimed to have seen two cases,

Hirschberg two cases, and similar cases were claimed to have been noted by Langenbeck, but Abadie¹ discards their claims, being unable to find published reports of their observations

In the discussion of Gangolphe's paper,⁹² Berard¹⁵ described a case of his own, which Stetten is inclined to accept as genuine, but which we have discarded as being too indefinite for acceptance. After describing a case occurring in mother and daughter, Guepin¹⁰⁴ reports a similar deformity in 14 other members of the family, while Feré⁸³ claims to have seen 25 cases in male epileptics. We are rather reluctant to embody these figures into our own statistics. We have found, as Stetten also remarks, considerable difficulty in knowing just which cases one should incorporate. In our own tabulation, we have tried to follow Stetten's criteria in rigidly rejecting all cases where

(1) There is a reasonable doubt as to the actual existence of a typical Madlung's deformity, and a probability that the condition was some other pathologic lesion

(2) The deformity was of such a slight degree that it could scarcely be considered abnormal

(3) The description was too vague or the reference too indefinite to justify inclusion

Also tending to upset an accurate statistical compilation is the occasional report of the same case by two men, as it occurs in the articles by Weber²³⁵ and Busch,³⁵ and Muller¹⁵⁵ and Franke⁸⁷. Stetten himself has reported the same case in two journals,^{220, 221} while it has been a common practice for several of the authors to rearrange their primary case report in subsequent articles

In view of the foregoing, we have attempted to eliminate these inaccuracies from the literature, and have compiled a chart tabulating 171 cases which we have succeeded in collecting

We cannot agree with Claiborne⁴³ in assuming that with the increasing number of examinations which are resulting from the Workmen's Compensation Act, and with the wider use of roentgenologic examinations in traumatic surgery, there will be more observations and reports of this condition, since the type of patient presenting a true Madlung's deformity does not come from either of these two groups. We do believe, however, that the condition is not so rare as the literature would seem to indicate, since it is not frequently recognized, especially without the aid of the roentgenologist

Case Report—Hosp. No. 69356 M. D. female age 18 was admitted to the Cumberland Hospital, January 31, 1938, to the service of Dr. G. B. Reitz, complaining of pain in and deformity of, both wrists during the past two years. She was born April 1, 1920, in the United States, and no history was obtainable of any birth injury having occurred. She had had measles, whooping cough and diphtheria. At age 9 she was struck by an automobile, but there was no history or evidence of any local injury to the wrists. She had not engaged in any particular occupation which might account for her deformity. Her mother, age 47, three sisters and two brothers are all living and well. Her father died of pneumonia at age 47. There were no deformities or any

indication of syphilis or rickets in either parent or in any of her five brothers and sisters.

Physical Examination revealed a well developed, well nourished girl, 160 cm tall, weighing 50 kg. Temperature 99.2°F , pulse, 84, respirations, 16, blood pressure, 130/65. The visible mucous membranes are of good color and the teeth are in good condition.

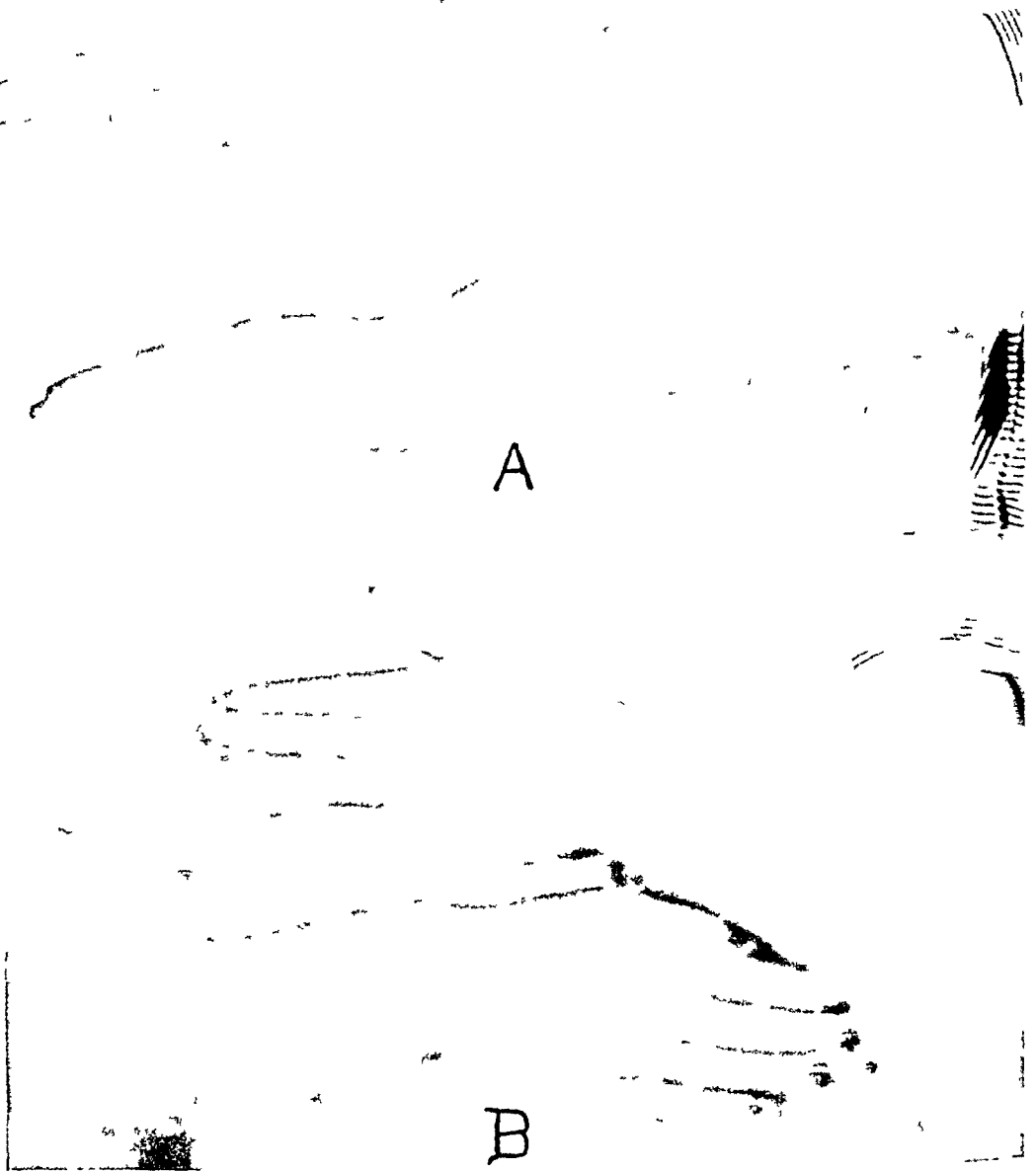


FIG 1—(A) Lateral view showing the characteristic bayonet shaped deformity and the shortening in the length of both forearms.
(B) Anteroposterior view showing the prominence of the head of the ulna at the back of the wrist and the ulnar deviation of the hand.

The organs of special sense, and the thoracic and abdominal viscera are all apparently normal, and there are no sensory, trophic or vasomotor disturbances. There are no frontal or parietal bosses, the thorax is well formed and there is no scoliosis, rachitic rosary or Harrison's groove. The hips and knees are normal and the tibiae are perfectly straight. There is no broadening of the epiphyses.

One is immediately struck by a curious bilateral deformity at both wrists (Fig 1 A

41	Sc	1	Con- cation of	Massage, electricity Bandaged in extension	—
42	Vel	1		None	Irreducible
43	Ve	1	algus, pes	None	Ulna reducible on pressure but recurs
44	Na	1		—	—
45	So	1		—	—
46	So	1	warfed, arum and	—	—
47	Pro	1	red and arum	—	—
48	Sch	1		Orthopedic apparatus	Course 4 yrs No im- provement
49	Put	1	and sco-	—	—
50	Put	1	us	Oblique linear osteot- omy of radius Plaster encasement	Course 1 yr Good re- sult
51	Sau	1	of the na Fun-	Avoidance of forced flexion Exercise	Deformity irreducible
52	Sau	1	and bi- arum	—	Course 1 yr
53	Stie	1		—	—
			De	Osteotomy of the	Good result



1

1

7



and B), as if the hands had been dislocated anteriorly. There is also an obvious shortening of both forearms (left—eight and one-quarter inches long, right—eight and one-half inches long). A lateral view of the forearm and hand roughly resembles a bayonet (Fig. 1 A). There is a marked swelling at the back of the wrist which palpation determined as being the head of the ulna and which, apparently, overrode the carpus superiorly. Palpation of the lower end of the radius reveals a definite forward bowing with convexity on the dorsal surface, and a moderate lateral bowing with the concavity toward the ulna. This bowing has displaced the carpus and hand forward and to the ulnar side. The flexor tendons are slightly more prominent than usual. Measurements of the forearms show

	Right	Left
Radius (from the head to the styloid process)	18 cm	18½ cm
Ulna (from olecranon to styloid process)	20½ cm	22 cm
Hand and forearm (olecranon to tip fifth finger)	32 cm	33 cm
Circumference of wrist (at styloid process)	16 cm	16 cm
Thickness of wrist (at styloid process)	4 cm	4¼ cm
Breadth of wrist (at styloid process)	5.8 cm	6½ cm
Humerus (from acromion to external condyle)	29½ cm	29½ cm

There is to be noted a decided shortening of the radius (from a normal of approximately 22 cm) of 4 cm on the right, and 3½ cm on the left, and also a shortening of the ulna (from a normal of approximately 25 cm) of 4 cm on the right, and 3 cm on the left. Motion is the same either active or passive, and is somewhat painful at the extremes. Mobility at the wrist is only slightly affected, and, although the deformity is clinically symmetrical, the right side is affected more than the left. The limit of motion from a horizontal plane is estimated as

	Right	Left
Flexion	90°	60°
Extension	30°	40°
Adduction	30°	40°
Abduction	25°	40°
Pronation and supination are within normal limits		

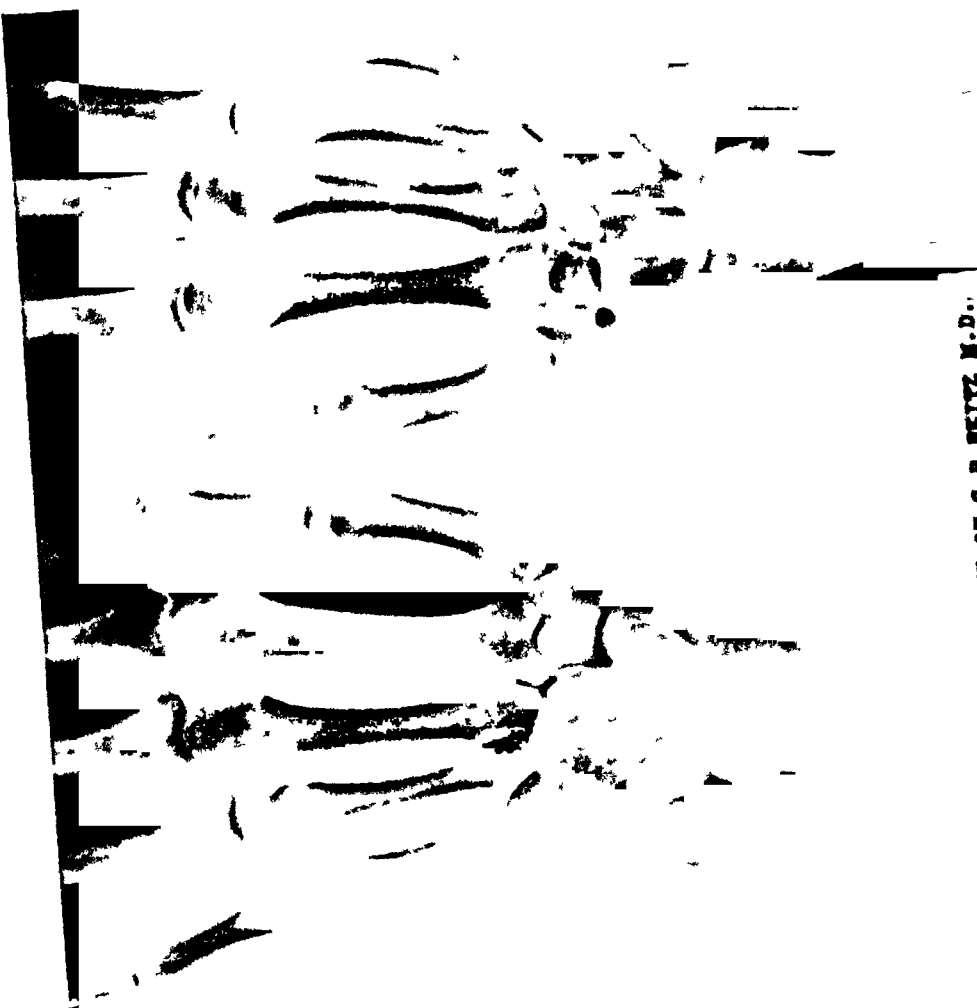
During a short stay in the hospital for the purpose of observation, a laboratory study of the patient was carried out. Similar studies, partial or complete, have been made by Beder,¹⁰ Brown,¹¹ Catterina,¹² Fazio,¹³ Siegrist,¹⁴ Stetten,¹⁵ Tollas,¹⁶ and Vianna.¹⁷ The results obtained by these investigations indicate that this condition is not manifested by any deviation of the body's chemical or biologic processes. The data acquired in the present instance tend to confirm that impression.

Laboratory Data—Wassermann test negative. Basal metabolism minus four. Urinalysis. Color—yellow, 1,015, alkaline, albumin, sugar, blood and bile, all absent. Microscopic examination essentially negative. Hematology. R B C, 5,030,000, Hb, 90 per cent, W B C, 8,950. Differential polymorphonuclears, 65 per cent, lymphocytes, 33 per cent, transitionals, 2 per cent, platelets 210,000, fragility, 0.45 to 0.27, sedimentation time, 18 Mm. in one hour and 20 minutes.

Blood Chemistry

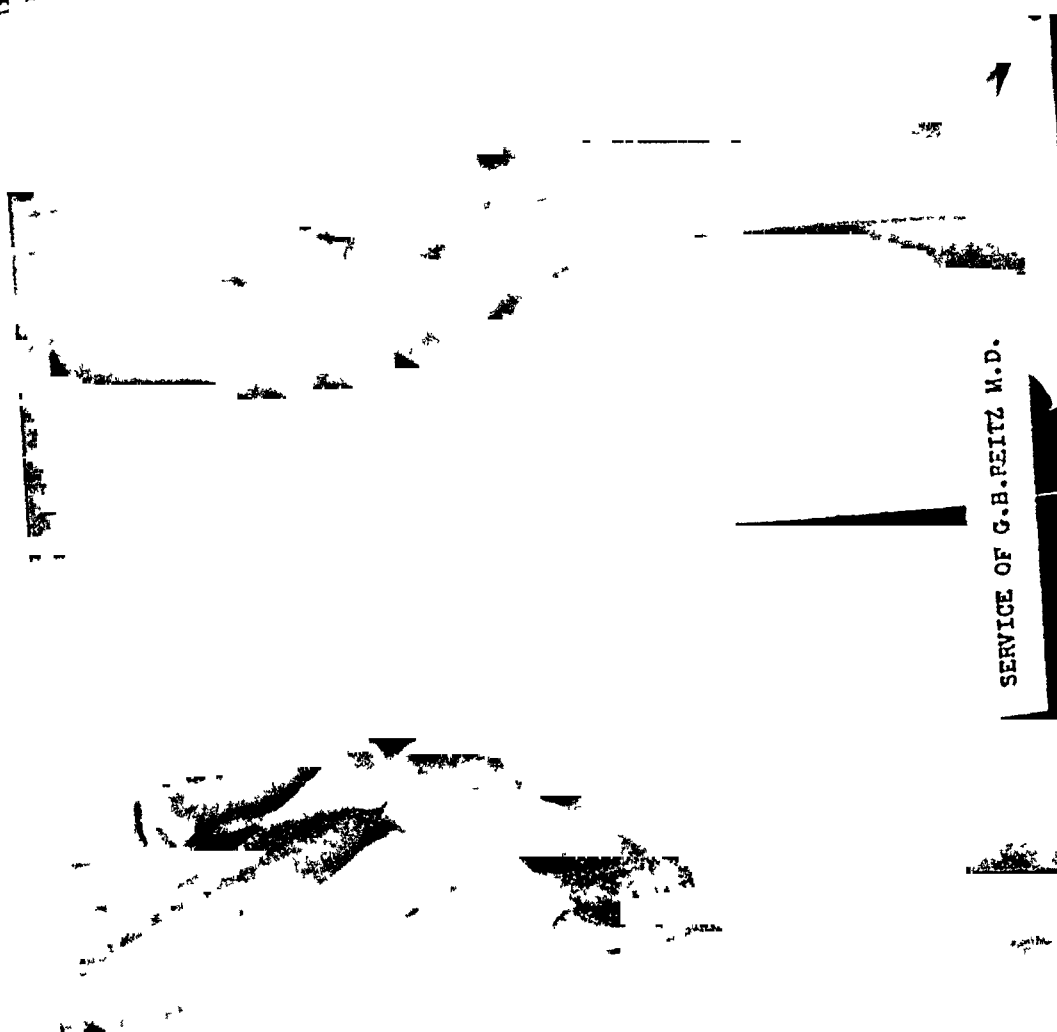
Urea nitrogen	12.9 mg	Total cholesterol	105.3 mg
Sugar	88.9 mg	Cholesterol ester	65 per cent
Albumin	9.3 mg	Calcium	10.5 mg
Globulin	2.2 mg	Phosphorus	4.8 mg
Chlorides	625.0 mg	Icteric index	3.8 m

van den Bergh Direct and indirect—negative



SERVICE OF G.B. PEITZ M.D.

FIG 1—Anteroposterior roentgenogram of the wrist and carpus showing the epiphyseal line and the absence of the capitol bones, the retraction of the medial border of the lower end of the radius.



SERVICE OF G.B. PEITZ M.D.

FIG 2—Lateral roentgenogram of the wrist showing the anterior bowing of the radius and the backward luxation of the head of the ulna.

Roentgenologic Examination—Dr G H Koiransky "There is a striking alteration in the relative lines of the radius and ulna on both sides, the tip of the ulna being on a definitely higher level than the styloid process of the radius. The epiphyseal line of the distal radial epiphysis is visualized on both sides only in its radial half, and instead of running transversely through the whole thickness of the radius, makes a sharp bend, almost at right-angles, in the cephalad direction. The articular surfaces of either radius, as visualized from lateral exposure, are definitely facing forward. The distal ulnar extremity is subluxated in the ulnar-dorsal direction. A small exostosis is noted on the ulnar aspect of the radius opposite the missing half of the epiphyseal line. The roentgenographic appearance is typical of the so-called Madelung's deformity" (Figs 2, 3, and 4). A roentgenogram of the skull (Fig 5) revealed "The character of the digital impressions are very marked, considering the age of the patient, and assume the appearance of the so-called '*luckenschadel*'". There is also evidence of a small amount of calcification in the region of the pineal body. The sella turcica is apparently normal in shape, size and appearance. Roentgenograms of the other long bones showed no abnormalities."

Because of the increased digital markings of the skull, it was desired to determine if there might be an increase of intracranial pressure. The patient, however, refused to submit to a spinal tap. Examination of the optic fundi did not reveal any papilledema.

In view of the fact that the patient presented no menstrual disorders, or any other evidence of a hormonal dyscrasia, it was not considered necessary to undertake the complicated determinations of the various sex hormones.

The patient was discharged and advised to return at a later date (on cessation of growth) for operative correction of the deformity.

PATHOLOGY—The data considered in determining the pathology of this condition were obtained by reviewing the 171 cases tabulated herewith, which we have accepted as authentic examples of the deformity. To earlier investigators^{89, 115, 135, 158, 192} the opportunity for necropsy diagnosis presented itself, and served to dispel the idea that the deformity was a dislocation of the hand. In 1897, Jagot¹¹⁴ first appreciated the importance of the roentgenologic examination in determining the diagnosis and pathology of this condition, and this aspect has been progressively developed, as evidenced by the increasing prominence given it in literature.

A review of the published articles reveals that this deformity of the wrist may affect any, or all, of the various structures that go to make up the wrist joint, but it is the *radius*, especially its lower extremity, that is essentially the seat of the primary pathologic phenomenon which is in the nature of an osteochondritic dysplasia, while any abnormalities of the ulna, carpal bones, articular cartilages, ligaments and tendons about the joint, are apparently all of a compensatory nature and secondary to the deformity of the radius.



FIG 4—Roentgenogram of the entire forearm showing an increase in the normal lateral curvature of the radius, the rarefied area on the internal margin of the lower end of the radius, and the exostosis on its ulnar border.

The Radius—There is a variable widening of interosseous space, due to an exaggeration of the usual, normal lateral curvature of the diaphysis. The most important disturbance is the palmar bowing of the distal end of the radius, usually in the lower third, its greatest degree being situated at the region of the epiphysis or metaphysis, sometimes as if the epiphysis itself had rotated (Fig. 6).

Kirnisson,¹²² Stetten,²⁰⁻²¹ Peckham and Hammond,¹⁶⁶ Gaudier,⁹⁶ and Burrows¹¹ have each reported a case where the usual anterior bowing is



FIG. 5—Roentgenogram of the skull showing a marked increase in digital impressions, calcification of the pituitary body, and a normal sella turcica.

reversed. These constitute the only five authentic cases of posterior bowing or "reverse" type of the deformity (Fig. 7).

The epiphysis has been described as irregular, scalloped and under- or overdeveloped. The epiphyseal line sometimes is found to be broadened, hazy, or entirely absent. If the roentgenograms are examined carefully, it can frequently be appreciated that the epiphyseal line is present only in its lateral half, and its absence in the inner, or ulnar half, is indicative of premature, partial fusion of the shaft and epiphysis. This finding will be noted in the roentgenograms illustrating the present case report.

Another interesting fact, brought out by Rocher¹⁹⁵ and stressed recently by other French authors,^{39, 194, 196, 197, 198, 202} is a hemiatrophy of the internal

half of the radial epiphysis. This is indicated on the roentgenogram by a small, rarefied area on the internal, or ulnar side of the radial shaft, immediately above the missing half of the epiphyseal line. This finding was also present in the case herewith reported, and was especially marked on the left side.

DIAGRAMMATIC SKETCHES ILLUSTRATING THE ANATOMIC RELATIONS OBTAINING IN MADELUNG'S DEFORMITY IN BOTH THE APPARENT ANTERIOR AND POSTERIOR ("REVERSE") DISLOCATIONS

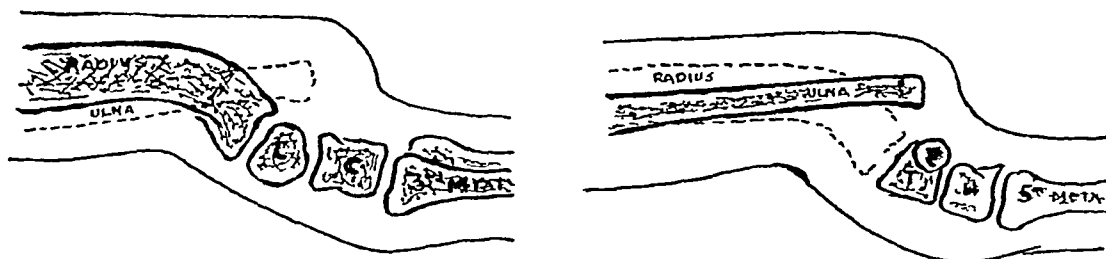


FIG 6—Showing the deformity at the back of the wrist, the bowing of the radius and the apparent anterior dislocation. (A) Section through the radius. (B) Section through the ulna.

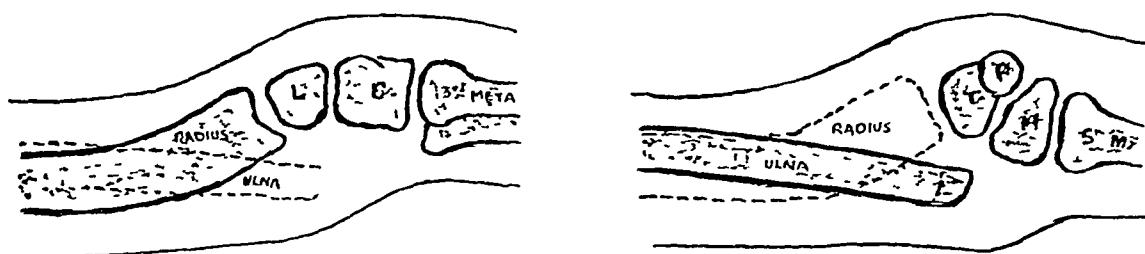


FIG 7—Showing the apparent posterior dislocation of a "reverse" Madelung's deformity. (A) Section through the radius. (B) Section through the ulna.

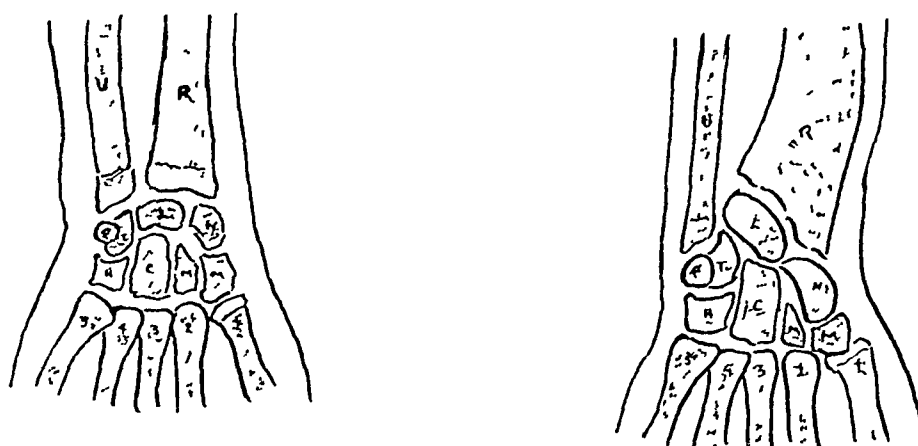


FIG 8—(A) Showing the normal arched arrangement of the carpal bones. (B) Showing the "pyramidalization" of the carpal bones in Madelung's deformity, with the os lunatum at the apex.

A third interesting fact, which Stetten²²¹ describes "as a remarkably frequent finding as a coexisting lesion," is the discovery of an exostosis near the distal epiphyseal line, usually on the ulnar side. These three factors are emphasized, and their significance will be appreciated in the consideration of the pathogenesis.

In addition to any apparent shortening of the total length of the radius due to an anterior or lateral curvature, the radius often suffers an actual

shortening in length, and the patient presents obviously fore-shortened fore-arms.

The Ulna - Although slight bowing and shortening of the ulna has also been occasionally described, this is never more marked than the radius rarely even as much. More usually the ulna grows toward, unaffected by the pathologic radius, thereby leading to a luxation or subluxation of the inferior radio-ulnar articulation. Most descriptions state: "The ulna is dislocated backward from the radius." Reicher, however, has pointed out that, strictly speaking, it is the radius - and not the ulna - which is dislocated. A hyperostosis of the ulnar head is a common finding.

The bowing and shortening of the radius result in the ulna overriding the carpus dorsally. This gives rise to the most prominent sign of the deformity - swelling at the back of the wrist due to the prominence or projection of the ulnar head or styloid. Since the ulna is now at a higher level than the hand and carpus, it gives one the impression of an anterior dislocation. In the "reverse" type of the deformity the ulna projects below the palmar surface of the wrist and results in the appearance of an apparent posterior dislocation of the hand and carpus. The end of the ulna may be forced back into position by cases of mild luxation, but the dislocation returns on release of pressure. The radial deformity cannot be reduced by manipulation since the deformity is an integral part of the bone.

The Radiocarpal Articulation - Considering the fact that the radius is deformed in such proximity to the wrist joint it is inevitable that in direct proportion to the degree of deformity, the wrist joint will be modified anatomically and functionally. Since the lower end of the radius which goes to make up the proximal half of the joint has been bent inward (due to lateral bowing) and downward (or upward in the "reverse" type), the articular surface of the lower end of the radius comes to face downward and somewhat ulnarward, instead of directly forward. Siegrist¹² describes this as "a deviation of the joint surface on two axes" and his article gives a comprehensive discussion of the mechanics of the modified joint.

Since the inferior radial articulation faces downward instead of directly forward, an anterior displacement of the hand and wrist takes place. There is no true luxation of the joint whatsoever, since the lunate and navicular bones retain their normal relationships to the articular surface of the radius.

Mobility at the joint is modified by the disturbance of mechanical factors. Thus the anterior bowing of the radius leaves the joint with an apparently hypertrophied superior lip thereby limiting extension somewhat. The seeming compensatory atrophy of the inferior lip often augments the range of flexion. In the "reverse" type of bowing the converse is present and flexion is found to be limited. Depending on the amount of lateral bowing adduction is variably restricted. The position of the ulna largely decides what range of abduction may take place. Usually the projecting end of the ulna acts as a splint along the lateral border of the carpus, greatly restricting abduction. Occasionally the projection may so disorganize the lateral side of the joint

that the carpal bones are forced into permanent adduction, and render abduction impossible

Although the pivot of pronation and supination is at the proximal radio-ulnar joint, both of these motions, particularly that of supination, are variably limited because of (1) The luxation at the inferior radio-ulnar joint (2) The bowing of the radius (3) The disparity in size between the radius and ulna

It is obvious, therefore, that restrictions, limitations and exaggeration of motion about the wrist are directly dependent upon bony impingements. A laxity of the joint membranes and ligaments, which has been a constant finding on dissection, is a negligible factor. Outside of the fact that the flexor tendons are rendered more prominent by being drawn taut over the inferior margin of the articular surface, they do not enter, essentially, into the pathology of this deformity

The Hand and Carpal Bones—The deviation of the articular surface inward leads to a modification of the usual arched arrangement of the carpal bones, which become wedged in between the deformed radius and the protruding ulna, assuming a triangular appearance, with the os lunatum at the apex (Fig 8). Benneke¹¹ described this "pyramidalization" of the carpal bones as compensatory to the malarrangement of the component parts of the wrist joint. Slight irregularities of the individual carpal bones have been described

When the course of the deformity has reached its culmination, the hand and carpal bones come to lie at a lower level than that of the ulna, the hand and forearm assuming a curious and characteristic "bayonet-shaped" deformity (Fig 1[A]). This has been persistently described as a "silver-fork" ("*gabel-hand*," "*manus furca*") deformity, but it is obviously a misnomer, as can be seen by viewing the wrist from the side. The exception would be those rare cases of the "reverse" type of the deformity, which is really a "silver-fork" deformity. It was probably Stetten's^{220, 221} report describing a case of this type that prompted subsequent authors to misapply that name to the usual deformity

Of the 171 cases herewith tabulated, it will be noted that the deformities were bilateral in 127 cases, of which 35 were more marked on the right and 21 more marked on the left. Two reports did not state whether a bilateral or unilateral condition existed. Forty-two unilateral cases are reported, of which 18 occurred on the right and 22 on the left side, while in two reports, the side affected was not specified. When both sides are involved, one side usually becomes deformed before the other

PREDISPOSING FACTORS—*Sex Incidence*—The influence of sex is indisputable—females predominating. The ratio of female cases to male is variably put at 2:1 by Madelung,¹³⁵ 3:1.8 by Abadie,¹ 4:7.9 by Homuth,¹⁰⁹ 7:1 by Stetten,²²¹ and 4:1 by Salisachs.²⁰³ Analysis of the 171 cases considered in Table I shows a ratio of 137:33 (one not specified), or an approximate ratio of 4:1

Age Distribution—This condition is, essentially, an affection of adolescence,

ETIOLOGIC THEORIES—The following theories have been advanced explaining the etiology of Madelung's deformity, some of which are no longer tenable, but are included for the sake of historic completeness

(1) *Trauma*—This factor was advanced by the old French school (Bégin,¹¹ Dupuytren⁷³) Along with the predisposing factor of occupation, trauma has been dropped from serious consideration for much the same reason—its preponderant occurrence in young girls, who are certainly less exposed to trauma than the general population

(2) *Muscular*—Madelung¹³⁵ himself, gave credence to this theory when he stated "The main factor in its causation is the more powerful action of the flexors of the forearm, due to overexertion Continued hyperflexion stretches the extensor tendons and the posterior ligaments over the dorsum of the radial epiphysis, exerting a forward force and producing a volar bowing" Busch,³⁵ who championed this theory, attempted to correct the deformity by tenotomy of the flexor tendons, but the procedure proved to be ineffectual This theory could hardly explain those cases of posterior bowing, nor does it take into account the anatomic position of these muscles and the insertions of their tendons, which would lead one to expect deformity to take place in the fingers and hand, rather than at the wrist

(3) *Nervous*—This theory, advanced in a hypothetic manner by Félix,⁸¹ is altogether untenable, and is merely mentioned in passing

(4) *Osseous Dystrophies*—Landivar¹²⁵ compares the deformity to the group of conditions such as Paget's or von Recklinghausen's disease, *etc*, but these conditions are each of their own clinical entity, and occasionally, if they should present a "symptomatic" form of Madelung's deformity, as in Björkroth's²³ or Rocher's¹⁹³ case, they may be easily differentiated roentgenologically

(5) *Inflammatory*—Considering the fact that osteomyelitis, as well as Madelung's deformity, also frequently occurs during the secondary growth period, and that Rosenow has succeeded in demonstrating organisms specific for various parts of the body, it is surprising that this theory has had such fleeting and ineffectual backing However, this is due to a lack of any positive evidence in its favor

(6) *Endocrine*—It is inevitable that the preponderance of female cases would suggest an endocrine basis for the condition Earl,⁷⁴ Cseréy-Pechany,⁵¹ and Beder¹⁰ have reported cases of the deformity which showed mild or severe ovarian hypofunction Cseréy-Pechany gave his two patients ovarian and glandular hormone therapy for a period of seven months He not only claimed to have checked the course of the disease, but attempted to demonstrate roentgenologically an actual regression of the deformity However, the course of the disease may cease at any time, even without medication, just as spontaneously and as insidiously as it began As for the roentgenographic evidence, one must realize that, unless serial exposures are made at exactly the same angle, marked differences in the appearance of the curvature may result

(7) *Rickets*—This theory has been regarded as the most frequently pro-

occurring in the secondary growth period, and has its inception, with but few exceptions, between the ages of ten and 14

Heredity—Definite instances of a hereditary influence are to be noted in nearly one-third of the reported cases. Guepin¹⁰⁴ reported a case of a girl whose mother presented an even more marked deformity, the father also had large wrists, the sisters and brothers of the mother showed a similar lesion, all nine sisters and brothers of the patient and the children of a sister had had prominent ulnae from childhood. In Jagot's case,¹¹⁴ the father, uncle, and grandfather had thickened wrists, but did not have any functional disturbance. Other instances of the deformity in three generations are to be found in the reports of Roget²⁰⁰—mother and grandfather, Volkmann²³⁴—mother and grandmother, Siegrist²¹²—sisters, mother and grandmother, and Reich¹⁸⁸. Cases occurring in siblings have been described by Ardouin⁷—brothers, Solberg²¹⁴—brothers, whose parents were cousins, Sauer²⁰⁴—brother and sister, Pedrazzi¹⁶⁷—mother and sister, Vidal²³²—mother and sister, and Wery²³⁶—sister. Not infrequently the deformity is present in mother and daughter, as cited in the reports of Dekeyser,⁵⁹ Gangolphe,⁹² Malfuson,¹³⁷ Levyn,¹³² and in Stetten's case,²²¹ where there was a history of deformed wrists in the mother. Other instances of a hereditary nature are found in the reports of Estor,⁷⁷ Brlandes,²⁶ Salisachs,²⁰³ Gaugele,⁹⁸ Magnus,¹³⁶ and Massabuau.¹⁴³ Nove-Josserand, in the discussion of Gangolphe's⁹² paper, suggests that a latent heredity, becoming active when the hands are first actively used, may be the etiologic factor of the deformity.

Occupation—This factor was once stressed by the early French writers, but it is illogical to suppose that any condition occurring usually in young girls who are either too young to work or whose work is of a comparatively light nature can claim occupation as an etiologic factor.

Environment—The high percentage of cases reported from the poorer classes can be easily explained by the fact that it is this class of patients that supply the clinical material upon which most of our medical literature is based. It was the opinion of the early writers that living conditions provided an etiologic factor to the development of this condition comparable, possibly, to the occurrence of rickets, tuberculosis, etc.

PATHOGENESIS—The multiplicity of nomenclature designating this condition reflects the variable pathologic processes propounded, and it has been remarked that there are nearly as many etiologic theories as there are authors. As examples, the following are instructive: "Manus valga" (Madelung, Siegrist and Sauer), "carpus curvus" (Delbet), "radius curvus" (Destot, Gangolphe), "congenital dislocation of the wrist" (Pooley, Estor), "late rickets of the wrist" (Duplay, Salisachs), "progressive subluxation of the wrist" (Kirmisson), "progressive idiopathic curvature of the radius" (Stetten), "adolescent club-hand" (Mauclair), "carpo-cyfose" (Robinson et Jacoulet), "cubitohisthesis" (Palazzi), "manus furca" or "gabelhand" (Springer), "radius brevior" (Masmontel), and "dyschondroplasia of the inferior radial epiphysis" (Rocher).

ETIOLOGIC THEORIES —The following theories have been advanced explaining the etiology of Madelung's deformity, some of which are no longer tenable, but are included for the sake of historic completeness

(1) *Trauma* —This factor was advanced by the old French school (Bégin,¹¹ Dupuytren⁷³) Along with the predisposing factor of occupation, trauma has been dropped from serious consideration for much the same reason—its preponderant occurrence in young girls, who are certainly less exposed to trauma than the general population

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(7) *Rickets* —This theory has been regarded as the most frequently pro-

pounded and ardently defended of all. A canvass of the literature reveals a comfortable majority as proponents of the etiologic factor of tardy, or late, rickets. Salisachs²⁰³ is a contemporary exponent of this theory, and a large part of his article is devoted to an attempt to prove its applicability. In rebuttal, we would like to point out that rickets is a constitutional disease, and shows other manifestations besides bony pathology, which are never seen in Madelung's deformity, nor have there been more than one or two cases in all those reported of the condition where other bony manifestations, such as craniotabes, Harrison's groove, rachitic-rosary, etc., have been demonstrated. The occasional coexistence of scoliosis can be explained on the ground of posture, nor is it unusual to find scoliosis coexisting with practically any study made of dispensary patients. The actual existence of rachitis tarda as a clinical entity has been denied by several authors (Holt¹⁰⁸), but even if one were to presume its existence, it would be difficult to explain how it would localize itself to one or both radii, to the exclusion of the rest of the skeletal system, since even those authorities who do believe in the existence of late rickets (Clutton,⁴⁵ Roose²⁰¹) insist that general epiphyseal lesions are essential for a diagnosis.

(8) *Dyschondroplasia of the Distal Radial Epiphysis*—Even Madelung, in his original presentation, presupposed "a primary weakness of the bone" in the etiology of the deformity, while Redard¹⁸⁶ expounded the idea that the disease was due to a disturbance of growth of the epiphyseal cartilage. Delbet⁶⁰ also concluded that it was due to an irregular development of the epiphyseal cartilage, related to cartilagenous exostosis, analogous to genu varum, but, like Redard, he imputed it to late rickets. Stetten²²¹ states that "Closer to the correct solution comes the suggestion that the deformity is a disease of the epiphyseal cartilage," and rejects entirely the factor of late rickets.

The mechanism of dyschondroplasia is suggested by the rarity of cases, the remarkable uniformity of the age at the onset, the usual bilateral occurrence, the absence of the usual stigmata of rickets or a history of local trauma, its onset during the secondary growth period, and the frequent association of the deformity with other anomalies. Kun¹²⁴ and Ingber¹¹² report the coexistence of an asymptomatic sacralization of the fifth lumbar metamere, Kajan,¹¹⁰ an homolateral cervical rib, Beder,¹⁰ Brown,³¹ Stokes,²²³ Mathieu,¹⁴⁵ von Bergmann,¹⁷ and Chierici,⁴¹ bowing of the tibiae, Rocher,¹⁹⁷ absence of the caput humerus, Kun¹²⁴ and Vianna,²³¹ spina bifida occulta, von Bergmann¹⁷ and Melchior,¹⁵¹ brachymetacarpals, Solberg,²¹⁴ Franke,⁸⁷ and Fazio,⁸⁰ stunted growth or dwarfism, Gadrat,⁹⁰ Curtillet⁵² and Dimitriu,⁶⁹ multiple exostosis. Possibly if all the cases reported were to have had the entire skeleton examined roentgenologically, numerous other osteochondritic anomalies would have been discovered.

Bessel-Hagen¹⁹ has attempted to demonstrate an arrest in the development of any bone which gives rise to exostosis formation. Stetten²²¹ remarks on the frequency of finding an exostosis near the distal epiphyseal line as a coexisting lesion in Madelung's deformity. The case herewith reported

presents this lesion, which may be noted on the ulnar side of the radius, at the level of the missing epiphyseal line (Fig 3) According to the observations of Bessel-Hagen, this would lead to an arrest of development on that side, which is apparently what happens The lateral side of the radius continues to grow at the epiphysis, sweeping the outer margin of the radius along an arc, thereby giving rise to the lateral bowing of the radius This lateral curvature was stressed particularly by Duplay,⁷² who ascribed it to rickets

If, as we are inclined to believe, the formation of the exostosis is secondary to, or part of, a premature fusion of part of the epiphysis with the diaphysis, there will result a local cessation of growth Growing ends of bone are known to receive their blood supply from four sources (1) The large nutrient artery which supplies the diaphysis, (2) a comparatively small epiphyseal artery, (3) the periosteal vessels, which supply the cortex, and (4) the juxta-epiphyseal vessels, as described by Lexer, which supply the growing metaphysis

Thus, with premature fusion of part of the epiphysis, this last source of nutrition is cut off, and its loss is indicated by a comparatively rarefied area of bone This rarefied area, to be found on the ulnar half of the radius, just above the epiphyseal line, is well shown in Figure 3, and has been repeatedly stressed by Rocher^{194, 195, 196, 197, 198} and by Canton³⁹

The hypothesis of local and partial fusion of only a section of the epiphysis can be deduced from the frequent finding that the epiphyseal line is indistinct, or even partly missing, as is shown in Figure 2 If we apply the same train of thought to early fusion of the volar half of the inferior radial epiphysis, we can see that the anterior bowing of the radius may be the result of local "achondroplasia," and that the mechanism of anterior bowing is dependent upon cessation of growth in the volar half of the epiphysis This is far more logical than the usual hypothesis, promulgated by Gangolphe,⁹² that the pressure of flexor action leads to an atrophy of the anterior half of the epiphyseal cartilage, with a compensatory hypertrophy of the posterior half

Pels-Leusden¹⁶⁵ also presented the hypothesis that a disease of the intermediary cartilage caused premature ossification of the ulnar and volar side, with a change in the direction of longitudinal growth Gickler¹⁰² proposes to explain this premature partial fusion on the ground of a hemorrhage into the metaphysis as a result of disease, weight-bearing (as in crawling about in infancy), slight trauma, or even rickets Hemorrhage would tend to cut off the local blood supply and lead to early fusion Redard¹⁸⁶ had previously observed that continuous irritation, such as might be received from performing some particular kind of work (washing, wringing, *etc*) produced a functional hyperactivity of certain portions of the cartilage

Fick and Pahl⁸⁴ point out that the dyschondroplasia itself is the basic factor, and any curvature produced is merely accidental, depending upon the portion of the epiphysis which undergoes dyschondroplasia Cases have been reported by Gickler,¹⁰² and Dee⁵⁷ where no bowing of the radius existed, but where

dyschondroplasia was present. Any early fusion due to dyschondroplasia will give rise to an actual shortening in the length of the radius.

We mention, in passing, that the mechanism of bowing in the rarer "reverse" type of the deformity is the premature fusion of the dorsal half of the radial epiphysis leading to posterior bowing. Stetten²²¹ considers the site of bending of the radius dependent upon the age at which the disease begins, the nearer the lower end of the shaft, the later the affection. Where the entire radius is curved, the process must have begun during intra-uterine life, although a visible deformity may not have been noted until the deformity reached its height. The degree of curvature would depend upon the activity of the pathologic process.

DIFFERENTIAL DIAGNOSIS—From the foregoing description, it would seem to be quite easy to diagnose this condition, but the large number of similar and secondary deformities which have been improperly introduced into the various bibliographies belies that ease. It is quite possible that fracture, dislocation, arthritis deformans, osseous dystrophies, tumor formation, *etc.*, might produce the bayonet-shaped deformity itself, but a careful history should elicit the spontaneous, idiopathic onset of the disease during the secondary growth period, its progressive nature giving an early clue to the diagnosis. A complete physical examination will reveal an absence of rickets and other general, or local, disturbances. A roentgenologic examination of the lesion would seem necessary to rule out a "symptomatic" form, and would definitely confirm the diagnosis beyond a doubt.

Those authors who have reviewed the literature extensively are almost unanimous in expressing a plea to separate the genuine Madelung's deformity from a "pseudo,"⁴¹ "spurious,"¹⁵³ "symptomatic,"²³ "simulating,"⁷⁰ "atypical"²²⁸ or "similar conditions,"³⁴ and other unrelated types of deformity of the wrist which have masqueraded into the literature of the true variety. Several authors, in deploring this hegira from specificity, have attempted to correct it by adding still more to an already overburdened nomenclature. Zeitlin²³⁹ suggests "Madelung's disease" (*morbus Madelung*), but Madelung has already given his name to a disease characterized by a diffuse symmetrical lipomatosis, or deposit of fatty tissue, on the upper part of the back, shoulders and neck. Burrows³⁴ suggests "Madelung's syndrome," but a deformity is not, strictly speaking, a "syndrome," and it has all the faults of eponymous nomenclature.

In condemnation of the pernicious custom of applying a person's name to a pathologic condition or operation, often undeservedly, we would suggest that Madelung's name be dropped. Sir Jonathan Hutchinson¹¹⁰ has remarked "So in pathology we have to contend against the tendency to substitute a name, or a definition, for the perception of an essential nature. As it is easier for us to worship a name, or even a book, rather than to conceive of a nonmaterial power, so we more readily become accustomed to content ourselves with some euphonious name for a disease, rather than to acquire the habit of constantly trying to realize its nature and its relation to possible causes."

The Standard Classified Nomenclature of Disease²¹⁹ has a system of

nomenclature based on both a topographic and an etiologic factor. Following their method of classification, Madelung's deformity would be indexed 23132-077 (that is distal radial epiphysis—dyschondroplasia of) and we therefore suggest calling the deformity "Dyschondroplasia of the Distal Radial Epiphysis."

Several writers, with whom we are inclined to agree, place this deformity among the better known, but equally cryptogenic, group of conditions which includes Perthe-Calvé-Legg's, Osgood-Schlatter's, Kohler's, and Keinboch's diseases. We suggest that these diseases be classified under the head of dyschondroplasias, and that they be renamed, as, for example, dyschondroplasia of the caput femoris instead of Perthe's disease, or scaphoid dyschondroplasia instead of Kohler's disease, *etc*.

Berg¹⁶ and Ewald,⁷⁹ among others, challenge the right of Madelung's deformity to be considered a clinical entity, and advance the opinion that the deformity is merely the sign of some underlying pathology—such as rickets, lues, osteitis deformans, *etc*.

Classifications of Madelung's deformity have already been advanced by Abadie,¹ Barthés,⁹ Depage,⁶⁴ Gasne⁹⁵ and Stetten.²²¹ It would seem advantageous, considering the present state of the literature, to formulate a classification that will include all the various types of the deformity, including the secondary static types. The following classification is, therefore, presented.

A Presenting Radial Deformity

- (1) With anterior bowing of the radius
 - (a) Radial dyschondroplasia (genuine Madelung's deformity)
 - (b) Secondary static deformity. Traumatic,^{70, 237} luetic,⁷⁶ inflammatory,^{64, 21} tuberculous,³⁸ osteitis,^{223, 193} rickets,⁹¹ *etc*
- (2) With posterior bowing of the radius
 - (a) Radial dyschondroplasia ("reverse" Madelung's deformity)
 - (b) Secondary static deformity¹⁵⁰
- (3) Without bowing
 - (a) Radial dyschondroplasia^{57, 102}
 - (b) Secondary static deformity

B Presenting Ulnar Deformity

- (a) Ulnar dyschondroplasia²³⁸
- (b) Secondary static deformity¹⁶²

PROGNOSIS AND TREATMENT—Pain may be present as long as the pathology progresses, but ceases when growth is arrested at the wrist, usually before the age of 25. The patient may then be educated in the better use of the deformed wrist.

Treatment at least up until the cessation of growth, should be palliative and consists in resting the part. This may be effected by splints, braces, or a plaster encasement, but these measures will not correct the deformity, nor will they prove effective in halting the progress of the disease. Tenotomy of

the flexor tendons of the forearm is unjustifiable, and the mere removal of the distal end of the ulna is also condemned

Osteotomy of the radius for the correction of the deformity has proven so effective, in competent hands, that it may be recommended routinely, just as one would in a case of badly bowed legs, malunited fracture, *etc*. In 1885, Duplay⁷¹ tried a transverse linear osteotomy, in 1904, an oblique type was advocated by Poulsen¹⁷⁸. Although these operations may suffice for mild forms of the deformity, most cases may necessitate a cuneiform osteotomy. The curve in the lower end of the radius is corrected, and a plaster encasement is applied, with the hand put up in extension and abduction. Springer,²¹⁸ advises that the hand be forced, if necessary, into supination (depronation). In order to hold the fragments more securely, Taylor²²⁵ inserted a metal plate.

When the ulna is markedly longer than the radius after the osteotomy, its projecting end must be resected in order to obtain a perfect functional result. However, since an osteotomy is liable to shorten an already stunted radius, Burrows³⁴ has devised an ingenious procedure wherein the resected head of the ulna is shaped and inserted as a bone graft, or peg, between the fragments of a linear osteotomy, thereby tending to conserve, or at times elongate, the length of the radius. The postoperative care is the same as for any osteotomy.

SUMMARY

(1) A typical case of Madelung's deformity is presented, the twenty-first to be reported from this country.

(2) The literature on this subject has been reviewed, and is found to be inaccurate, incomplete and is replete with reports of cases that are not genuine. An attempt has been made to correct these errors and to properly correlate the history of this condition.

(3) A tabulation of 171 authentic cases has been compiled.

(4) We advocate the substitution of the term "Dyschondroplasia of the Distal Radial Epiphysis" in place of "Madelung's deformity," since the latter term is not specific.

(5) A classification of the various types of the deformity has been formulated.

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WITH

INTRODUCTION OF REMARKS RELEVANT TO EACH ARTICLE

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- ⁹ Barthes, Louis Charles De la luxation progressive du poignet chez l'adolescent et chez l'adult These de Paris, 495, July 19, 1904 (Describes cases of Malgaigne, Gevaert, Guery, Lesauvage and Madelung Of his own two cases, one is probably exuberant callus after fracture of scaphoid, the other an unrelated type of contracture)
- ¹⁰ Beder, W L, und Heinismann, J I Zur Genese Madelung'schen Deformitat Fortschritt a d Geb d Roentgenstrahlen, 52, 595-601, December, 1935 (Two cases—Importance of endocrine (ovarian) dysfunction in the genesis of Madelung's deformity)
- ¹¹ Begin Radiocarpien Dictionaire des sciences medicales, 13, 491-498, 1825 (Description on page 493 of an occupational deformity)
- ¹² Begin Bull de l'Acad de Med de Paris, 6, 803, June 20, 1841 (Discussion of Scoutetten's²¹⁰ paper)
- ¹³ Benneke, E Uber einen Fall von sogenannter progressiver Luxation des Handgelenkes Verhandlungen der deutschen Gesellschaft fur Chirurgie, 31, 157-159, 1904 (1 case)
- ¹⁴ Bennett, William H A Case of Spontaneous Displacement Forward of Both Wrists Transactions of the Clinical Society of London, 25, 265-267, 1892 (Author evidently unaware of Madelung's report Two cases are suggestive of Madelung's deformity but only Case 2 is acceptable even though description is meager)
- ¹⁵ Bérard Description of a Case, in Discussion of Gangolphe's⁹² Paper Bulletin de la Societe de Chirurgie de Lyon, 2, 135, 1899 (Too meager for acceptance)
- ¹⁶ Berg, Peter Die Madelung'schen Deformitat des Handgelenkes Carpus valgus Archiv fur Orthop Mechan und Unfall-Chirurgie, 12, 325-338, 1913 (Case 1 accepted, Case 2 rachitic, Case 3 accepted)
- ¹⁷ von Bergmann Subluxation beider Hande Freie Vereinigung der Chirurgen Berlins, October 8, 1888, Deutsche medizinische Wochenschrift, 14, 861, 1888 (1 case)
- ¹⁸ Bertolotti, Orazio La malattia di Madelung o Cubitolistes posteriori La Medicina Pratica, 13, 95-99, March 1, 1928 (1 case)
- ¹⁹ Bessel-Hagen, Fritz Uber Knochen- und Gelenkanomalien, insbesondere bei partiellem Riesewuchs und bei multiplen cartilaginaren Exostosen (Uber angeborene und pathologische Luxationen des Radiuskopfschens) Archiv fur Klinische Chirurgie, 41, 420-435, 1891 (Presents no true cases of Madelung's, but points out relationship of exostosis formation)
- ²⁰ Bideau De la Maladie de Madelung These de Bordeaux, 1909 (Not obtainable)
- ²¹ Binet, Trenel, et Worms Les incurvations des os de l'avant-bras consecutives a l'osteomyelite de leur extremite inferieure Archives Med des Enfants, Paris, 13, 353-362, 1910 (Deformity secondary to osteomyelitis)
- ²² Binet, A, et Mutel, M Le Radius Curvus Revue de Chirurgie, Paris, 48, 567-584, 1913 (A case of generalized rickets)
- ²³ Bjorkroth, Torsten An Extraordinary Case of Deformity of the Wrist (Symptomatic Form of Madelung's Deformity) Acta Orthopaedica Scandinavia, 2, 242-252, 1932 (Not a true deformity)
- ²⁴ Bode, Otto Demonstration eines Falles von Spontanluxation der Hand Freie Vereinigung der Chirurgen Berlins, June 8, 1891, Berliner Klinische Wochenschrift, 28, 900, 1891 (1 case)

- ²⁵ Bode, O Ein Beitrag zur Aetiologie und Casuistik der Spontanluxation der Hand Berliner Klinische Wochenschrift, 28, 1128-1130, 1891 (Discussion)
- ²⁶ Brandes, Max Zur Madelung'schen Deformität des Handgelenkes Zeitschrift für Orthopädische Chirurgie, 28, 392-414, 1911 (3 cases)
- ²⁷ Bindeau, A Luxation congenitale du Radius Bull de la Soc d'Obstet de Paris, 11, 140-141, 1908 (Deformity of elbow)
- ²⁸ Blinnsmade, William B Madelung's Deformity of the Hands N Y Surg Soc, ANNALS OF SURGERY, 47, 794, 1908 (1 case)
- ²⁹ Bioca, August Radius Curvus La Tribune Medicale, Paris, 3, 759-760, 1905 (Discussion, no report)
- ³⁰ Broca, A Discussion sur la tuberculose inflammatoire (discussion on the report of Poncet et Leriche) ¹⁷⁴ Bull et Mem de la Soc de Chirurgie de Paris, 34, 1004-1005, July 29, 1908
- ³¹ Brown, George M Report of a Case of Madelung's Deformity Medical Clinics of North America, 6, 1313-1318, March, 1923 (1 case)
- ³² Bsteh, O Radiusfraktur bei Madelung'schen Deformität Zentralblatt für Chirurgie, 58, 1955-1957, 1931 (Traumatic case)
- ³³ Buimer, R, et Neveux, A Luxation bilaterale et symétrique de l'extrémité inférieure du cubitus en arrière avec radius curvus (Maladie de Dupuytren-Madelung et ses Variétés) Archives Générales de Chirurgie, 3, 805-817, 1909 (1 case, discusses different degrees of the deformity)
- ³⁴ Burrows, H Jackson Operation for the Correction of Madelung's Deformity and Similar Conditions Proceedings of the Royal Society of Medicine, 30, 567-572, March, 1937 (Cases 1 and 2 are Madelung's, Case 3 is inflammatory)
- ³⁵ Busch, Wilhelm Lehrbuch der Chirurgie, Berlin, 2, Part 5, 111, 1864
- ³⁶ Cabeça, Custodio Sub-luxação espontânea do punho, Carpus-curved Revista portuguesa de medicina e cirurgia praticas, 6, 51-58, 1899 (1 case)
- ³⁷ Callandra, E Sulla Radio-distrofia del Madelung Corso di lesioni di ortopedia Anno Accademico 1927-1928 (Not obtainable)
- ³⁸ Cantas, M Contribution à l'étude de la pathogenie de la deformation de Madelung ou Radius curvus, Sur un cas de maladie de Madelung ou Radius curvus d'origine tuberculeuse Lyon Chirurgie, 10, 434-469, 1913 (Tuberculous deformity)
- ³⁹ Canton, J Un cas de dyschondroplasie radio-cubitale inférieure avec hémiatrophie épiphysaire radiale Revue d'Orthopédie, 22, 58-62, 1935 (1 case)
- ⁴⁰ Catterina, A Contributo allo studio della malattia di Madelung La Chirurgia degli Organi di Movimento, 10, 517-532, April, 1926 (1 case)
- ⁴¹ Chierici, Romola Madelung e Pseudo-Madelung Quaderni Radiologici, 7, 3-24, 1936 (2 cases true, 2 pseudo)
- ⁴² Ciacca, S Luxation isolée palmaire du cubitus dans l'articulation radio-cubitale inférieure Archiv italiano di Chirurgia, 24, 125, 1924 (Dislocation, not Madelung's)
- ⁴³ Claiborne, E M, and Kuntz, T G Madelung Deformity with Report of a Case Radiology, 27, 594-599, November, 1936 (1 case)
- ⁴⁴ Clarke, J Jackson Acquired Spontaneous Subluxation of the Wrist Orthopedic Surgery, London, 216-217, 1899 (This frequently quoted text is brief and inaccurate)
- ⁴⁵ Clutton, N H On Adolescent or Late Rickets Lancet, 2, 1268-1271, 1906
- ⁴⁶ Cnopf Über Madelung's spontane Subluxation des Handgelenks nach vorn Festschrift für Hofrat Goschel, Tübingen, 1902, abstracted in Zentralbl f Chir, 30, 574-575, 1903 (1 case)
- ⁴⁷ Codet-Boisse, P Deformation symétrique des deux poignets du type Dupuytren-Madelung Revue d'Orthopédie, 2, 35-45, 1911 (1 case)
- ⁴⁸ Colle, G Luxations divergentes des têtes du radius et du cubitus Archivio italiano di Chirurgia, 15, 685-697, June 6, 1926, abstracted in Journal de Chirurgie, 28, 748, 1926 (Traumatic deformity)

- ⁴⁰ Cruvelhier Traite d'Anatomie Pathologique, Paris, 1849, 9 This case, described by Smith,¹³ is too indefinite for acceptance)
- ⁴¹ Crysospathes, d'Antrenes Zwei Falle von gegengleicher Madelung's Deformitat zugleich ein Beitrag zur Aetiologie derselben Arch fur Orthop Mechanotherapie und Unfall Chirurgie, 11, 328-338, 1912 (Cases of traumatic deformity)
- ⁴² Cserey-Pechany, Albin Beitrag zur Aetiologie und Therapie der Madelung'schen Krankheit Zentralblatt fur Chirurgie, 57, 774-777, March, 1930 Case 1—Generalized rickets, Case 2—Madelung's, possible ovarian origin and ovarian hormone treatment)
- ⁴³ Curtillet, J Quatre cas d'exostoses osteogeniques multiples hereditaires et familiales Revue d'Orthopedie, 3, 193-206, 1912 (Four cases having multiple exostoses Case 2 resembles "radius curvus" but is not specific enough for acceptance)
- ⁴⁴ Dalbera, Maurice La Loi d'Ollier Son application en pathologie notamment dans la maladie de Madelung et l'Hemimelie partielle These de Paris, 160, 1927 (Relation of Ollier's law to Madelung's deformity)
- ⁴⁵ David, Max Die Spontane subluxation des Handgelenkes Grundriss der Orthopadischen Chirurgie, Berlin, 121, 1900, 140, 1906 (Brief description but no new case report)
- ⁴⁶ Davoigneau, et Lehmann, R Trois cas de maladie de Madelung Societe Francaise d'electrotherapie et de Radiologie, October 24, 1923 La Presse Medicale, 31, 955, 1923 (Three cases are presented but, although suggestive, are too briefly described for acceptance)
- ⁴⁷ DeBernardi, Renato Contributo radiologico allo studio della deformità di Madelung La Radiologia Medica, 12, 393-398, 1925 (2 cases)
- ⁴⁸ Dee Spontaneous Luxation of Wrists—Madelung's Deformity Medical Journal of South Africa, 16, 158, 1920-1921 (Case of dyschondroplasia of the inferior radial epiphysis, but no bowing of radius)
- ⁴⁹ Define, Domingos Sobre un caso de deformidade de Madelung Annaes Paulistas de Medicina e Cirurgia, 15, 237-245, 1924 (1 case)
- ⁵⁰ Dekeyser, Arthur Subluxation spontanee du poignet, Subluxation de Madelung Journal Medicale de Bruxelles, 6, 593-597, 1901 (2 cases)
- ⁵¹ Delbet, Pierre Carpus Curvus Leçons de clinique chirurgicale faites à l'Hôtel Dieu, Paris, Aug-Sept, 1897 Paris, 161-190, 1899 (1 case, excellent discussion)
- ⁵² Delitala Sulla malattia di Madelung XIX Congresso della Societa Italiana di Orthopedia, October 10, 1928 La Riforma Medica, 44, 1498, 1928, La Clinica Chirurgica, 31, 1256, 1928 (Description of two cases, too meager for acceptance)
- ⁵³ Denucé et Rabere Subluxation progressive des poignets, Maladie de Madelung Journal de Medicine de Bordeaux, 38, 58-59, 1908 (1 case) These de Bordeaux, 1908 (Not obtainable)
- ⁵⁴ Depage, A Un cas de maladie de Madelung Societe Clinique des Hôpitaux de Bruxelles Journal Médicale de Bruxelles, 10, 673, 1905 (Not a true case of Madelung's, see ref 64)
- ⁵⁵ Depage, A Note clinique a propos de la subluxation du poignet ou maladie de Madelung Journal Medicale de Bruxelles, 11, 401-406, 1906 (Deformity due to inflammation)
- ⁵⁶ Ders Die Madelung'schen Deformitat der Hand Hospitalstidende, 33, Kopenhagen (Not obtainable)
- ⁵⁷ Destot, Etienne Traumatismes du poignet et Rayons-X Masson et Cie, Chapt vii, 1923, Luxations radio-carpienne (Fig 69 shows a roentgenogram of true Madelung's, but there is no case report See also Destot's note to Gangolphe's⁵² ⁵³ paper)
- ⁵⁸ Destot, Etienne Injuries of the Wrist, a Radiological Study Hoeber, New York, 1926 (English translation of the above text by Atkinson)

- ⁶⁹ Destot et Gallois Recherches physiologiques et experimentales sur les Fractures de l'extremite inferieure du Radius Revue de Chirurgie, 18, 886-915, 1898 (This is an excellent thesis on fractures, but makes no mention of Madelung's)
- ⁷⁰ Dimitriu, V Un cas rare de maladie de Madelung Journal de Radiol et d'Electrol, 18, 535-536, October, 1934 (Case is one of multiple exostoses of long bones)
- ⁷¹ Donovan, Ricardo F Deformacion traumatica radiocarpiana (simulando un caso de Madelung) Boletines y Trabajos de la Sociedad de Chirurgia de Buenos Aires, 16, 1405-1409, November 16, 1932 (Traumatic deformity)
- ⁷² Duplay, Simon De l'osteotomie lineaire du radius pour remedier aux difformites du poignet, soit spontanees, soit traumatiques Archives Generales de Medicine, 15, 385-395, April, 1885 (1 case)
- ⁷³ Duplay, Simon Un cas de rachitisme tardif des poignets Gazette des Hopitaux, 64, 1397-1398, 1891 (1 case)
- ⁷⁴ Dupuytren Leçons orales de clinique chirurgicale faites a l'Hôtel Dieu de Paris, 4, 209-210, 1834 (Describes occupational deformities)
- ⁷⁵ Earl, George Madelung's Deformity The Journal-Lancet, 36, 229-232, 1916 (1 case)
- ⁷⁶ Elmslie, R C Madelung's Deformity of Left Wrist Proceedings of the Royal Society of Medicine, 1921-1922, 15, Part III, Section Surgery, subsection Orthopedics, p 82 (Only mentions presentation of case No description warranting acceptance)
- ⁷⁷ Erlacher, Philip Gabelhand bei kongenitaler lues Beitrage zur Entstehung der Madelung'schen Deformitat Archiv fur Klinische Chirurgie, 125, 776-789, 1923 (Luetic deformities)
- ⁷⁸ Estor, E De la Subluxation Congenitale du poignet Revue de Chirurgie, 36, 145-168, 317-348, 1907 (1 case)
- ⁷⁹ Ewald, Paul Zur Aetiologie der Madelung'schen Deformitat Archiv fur Klinische Chirurgie, 84, 1099-1111, 1907 (Case is traumatic)
- ⁸⁰ Ewald, Paul Die Madelung'schen Deformitat als Symptom und als Krankheit sui Generis Zeitschrift fur Orthop Chirurgie, 23, 470-497, 1909 (9 cases of wrist deformity presented, only 1 (Case 7) may be accepted as Madelung's)
- ⁸¹ Fazio, Leonardo Sulla radiodistrofia del Madelung Archiv di Ortop, 44, 551-565, June 30, 1930 (1 case)
- ⁸² Felix, Joseph Étude sur la subluxation spontanee du poignet en avant These de Lyon, 246, 1884 (2 cases)
- ⁸³ Felix, W Beitrag zur Kasuistik der Madelung'schen Deformitat Zeitschrift fur Orthop Chirurgie, 49, 563-568, 1928 (Cases 1 and 2, traumatic, Case 3, rachitic, Case 4, true Madelung's—1 case)
- ⁸⁴ Fere, Ch Note sur les difformites de developpement du cubitus et de la clavicle Revue de Chirurgie, 16, 398-402, 1896 (1 case) (Claims to have seen 24 cases in epileptic patients, but these are probably traumatic and are too indefinite for inclusion)
- ⁸⁵ Fick, R, und Pahl, J Uber einen Fall von doppelseitiger Madelung'schen Fehlform des Handgelenks mit Berucksichtigung seiner Mechanik Archiv fur Klinische Chirurgie, 163, 499-518, 1931 (1 case)
- ⁸⁶ Finzi The Cause of Madelung's Deformity Seventeenth International Congress of Medicine, London, 1913, 7, Part 2, Orthopedics, 339-344 (1 case) La Presse Medicale, 21, 727, 1913 (Same case)
- ⁸⁷ Foschini, Domenico Contributo alla patogenesi della deformita di Madelung Giornale di Clinica Medica, 8, 510-513, August 31, 1927 (1 case)
- ⁸⁸ Franke Zur Anatomie der Madelung'schen Deformitat der Hand Deutsche Zeitschrift fur Chirurgie, 92, 156-180, 1908 (1 case, with dissection This is the same case as that by Muller¹⁴⁵)
- ⁸⁹ Frolich, M Radius Curvus ou Maladie de Madelung Revue Medicale de l'est, 1, 586-587, 1922 (Discussion on Mathieu's¹⁴⁴ ¹⁴⁵ case)

- ⁸⁹ Frolich, M Discussion on Finzi's⁸⁸ paper Seventeenth International Congress of Medicine London, 1913, 7, Part 2, Orthopedics, pp 344 (Case described is too indefinite for inclusion and is probably that of Mathieu and Joseph,^{144, 145} q v, upon which he operated) Also see La Presse Medicale, 21, 592, 1913 (Case 1, as above, Case 2 arthritis, Case 3, osteomyelitis)
- ⁹⁰ Gadrat, J, et Marques, Pierre Exostoses Osteogeniques multiples et main de Madelung Journal de Radol et d'Electrol, 19, 72-78, February, 1935 (Several cases of multiple exostoses of long bones, not typical of Madelung's deformity)
- ⁹¹ Gaillot, Gaston Henri Contribution a l'etude de Radius Curvus These de Lille, 18, 1907 (Case of generalized rickets)
- ⁹² Gangolphe Deformation singuliere du poignet inexactement denomnee subluxation spontane Bulletin de la Societe de Chirurgie de Lyon, 2, 117-123, 126, 135, 1899 (2 cases)
- ⁹³ Gangolphe Malformation congenitale du poignet Lyon Medicale, 90, 451, 1899 (Same cases as above⁹²)
- ⁹⁴ Garrido-Lestache J Un caso de enfermedad de Madelung La Pediastría Española, 14, 138-143, 1925 (1 case)
Gasne Ernest Deformation rachitiques tardives du poignet Subluxation de Madelung et Radius Curvus Revue d'Orthop, 7, 153-170, 241-260, 1906 (No case reports)
- ⁹⁵ Gaudier, H Deformation rachitique symetrique des deux poignets par radius curvus Revue d'Orthopedie, 10, 263-266, 1909 (1 case)
- ⁹⁶ Gaugele, Karl Madelung'schen Handgelenks Deformatat Archiv fur Klinische Chirurgie, 88, 1058-1075, 1909 (Cases 1 and 2, no bowing of radius Case 3, ref 98)
- ⁹⁷ Gaugele Karl Gibt es eine genuine Madelung'sche Handgelenks Deformatat? Zeitschrift fur Orthop Chirurgie, 24, 462-479, 1909 (4 cases, 3 are accepted, the fourth was rachitic)
- ⁹⁸ Gazzotti, L G Contributo al trattamento della deformita di Madelung La Chirurgia degli Organi di Movimento, 16, 263-273, July, 1931 (1 case)
- ⁹⁹ Gery de Chastenot et Colombier Deux cas de Radius Curvus Bull et Mem de la Societe d'Anatomie de Paris, 17, 370-376, 1920 (2 cases, with dissection of Case 1)
- ¹⁰⁰ Gevaert, G Un cas de subluxation du poignet de Madelung Revue d'Orthopedie, 2nd series, 3, 335-342, 1902 (1 case)
- ¹⁰¹ Gickler, H Wachstumsstorung der Radiusepiphyse und Madelung'sche Deformatat Archiv fur Orthop und Unfall Chirurgie, 33, 312-318, 1933 (4 cases of dyschondroplasia of the inferior radial epiphysis, but with no bowing of radius)
- ¹⁰² Greig, D M Congenital Dislocation of the Ulna Edinburgh Medical Journal, 31, 373-391, July, 1924 (1 case)
- ¹⁰³ Guepin, A Lavite congenitale de l'articulation radio-cubital inferieure et subluxation consecutive de la tete du cubitus en arriere Comptes rendus hebdomadaires des seances et memoires de la Soc de Biologie, 44, 627-631, 1892 (2 cases with a history of similar deformity in 14 members of the family)
- ¹⁰⁴ Guery, A Un cas de luxation progressive du poignet (Subluxation spontanee de Madelung) Revue d'Orthopedie, 9 277-282, 1898 (1 case)
- ¹⁰⁵ Guye Observation d'un cas de maladie de Dupuytren-Madelung bilaterale Revue Medicale de la Suisse Romane, 39, 191-192, April, 1919 (1 case)
- ¹⁰⁶ Hoffa, Albert Lehrbuch der Orthopadischen Chirurgie, 1st Edit, 486-488, 1891, 5th Edit, 510-511, 1905 (Text, no case report)
- ¹⁰⁸ Holt, C Emmet The Diseases of Infancy and Childhood 4th Edit, 268, 1908
- ¹⁰⁹ Homuth, Otto Die Madelung'sche Deformatat in ihrer Beziehung zur Rachitis Beitrage zur Klinischen Chirurgie, 74, 562-584, 1911 (Case of generalized rickets)
- ¹¹⁰ Hutchinson, Sir Jonathan Some General Remarks on the Series of Cases and on the Employment of Names (Archives of Surgery, London, 9, 26-27, 1898)
- ¹¹¹ Ianni, Raffaele Radius Curvus, Deformatat di Madelung-Duplay Annali Italiana di Chirurgia, 3, 40-61, 1924 (1 case)

- ¹¹² Ingber, E Bilateral Madelung Deformity and True Asymptomatic Sacralization of the fifth Lumbar Metamere, Roentgen Study of a Case *Quadern Radiologia*, 5, 251-257, 1934 (1 case, not obtainable)
- ¹¹³ Jacoulet, F Un cas de maladie de Dupuytren-Madelung *Revue d'Orthopedie*, 1, 35-42, 1910 (1 case)
- ¹¹⁴ Jagot, C Sur une vice hereditaire de conformation des deux poignets *Archives Med d'Angiers*, 1, 159-170, 1897 (1 case)
- ¹¹⁵ Jean, A Double luxation congenitale complete du cubitus et incomplete du radius sur les os du carpe *Bull de la Soc Anat de Paris*, 10, 398-400, 1875 (1 case, dissected)
- ¹¹⁶ Jones, S Fosdick Bilateral Congenital Dislocation of the Lower End of the Ulna *American Journal of Orthopedic Surgery*, 9, 199, November, 1911 (1 case)
- ¹¹⁷ Josa, Laszlo A csuklo Madelung-fele deformitasanak egy esete *Orvosi Hetilap*, 70, 1321-1324, 1926 (1 case)
- ¹¹⁸ Jouon, E Deformation de l'avant-bras par arrête developpement de l'extremite inferieure du cubitus, de cause inconnue *Revue d'Orthopedie*, 6, 81-84, 1905 (Case of ulnar dyschondroplasia with deformity of the radius)
- ¹¹⁹ Kajon, Cesar Madelung'sche Deformitat konbiniert mit Halsrippen *Wien med Wochenschrift*, 84, 460-462, April 21, 1934 (1 case with cervical ribs)
- ¹²⁰ Kieffer, Charles F Congenital Dislocation of Both Ulnae at the Wrists *ANNALS OF SURGERY*, 38, 119, 1903 (1 case)
- ¹²¹ Kassowitz, M Die Ursache der Gelenkschlaffheit der Rhachitis *Centralblatt fur Chirurgie*, 9, 385-390, 1882 (This much quoted article presents no cases nor mentions Madelung's deformity)
- ¹²² Kirrmisson, E Subluxation progressive du poignet Les deformites acquises de l'appareil locomoteur pendant l'enfance et l'adolescence *Masson et Cie, Paris*, 363-375, 1902 (1 case)
- ¹²³ Kolliker, Th Die Dupuytren'sche und Madelung'sche Deformitat des Handgelenkes Joachimstahl's Handbuch der Orthopadischen Chirurgie, 2, 34-37, 1907 (Text, no case report)
- ¹²⁴ Kun, Etienne Contribution a l'etude de la Maladie de Madelung These de Paris, 1933, 23 (Case 1, traumatic, Case 2, Madelung, Case 3, generalized rickets)
- ¹²⁵ Landivar, Adolfo F y Iparraguirre, and Cesar, A Leoni Radius Curvus bilateral de comienzo tardio *Bol y Trab de la Soc de Cir de Buenos Aires*, 20, 1160-1168, November, 1936 (1 case)
- ¹²⁶ Laurence, Joseph La Maladie de Dupuytren-Madelung *Revue Generale de Clinique et de Therapeutique, et Journal des Practiciens*, 37, 75, 1923 (Discussion)
- ¹²⁷ Leclerc Radius Curvus *Bulletin de la Societe de Chirurgie de Lyon*, 8, 115-120, 1905 (Same case as Albertin and Leclerc⁵)
- ¹²⁸ Lenormant, Ch Un nouveau cas de radius curvus *Revue d'Orthopedie*, 7, 1-10, 1907 (1 case)
- ¹²⁹ Leriche, R Sur un cas de Maladie de Madelung bilaterale Par lesion du cartilage de conjugaison radiale *Revue d'Orthopedie*, 10, 495-500, 1909 (1 case)
- ¹³⁰ Lesauvage, de Caen Memoire theorique et pratique sur les luxations dites spontanees ou consecutives et en particulier sur celles du femur *Archives Generales de Medicine*, 9, 257-284, November, 1835 (Case 1, on page 260, is a pathologic dislocation)
- ¹³¹ Levy, Richard Uber Madelung'sche Handgelenksdeformitat *Berliner Klinische Wochenschrift*, 45, 2213-2216, 1908 (Case of rickets)
- ¹³² Levyn, L Madelung's Deformity, A Report of Two Cases, Constituting the Fifth and Sixth American Cases *Radiology*, 3, 145-149, August, 1924 (2 cases)
- ¹³³ Llado, Antonio Cortes, y Gallardo, Louis Salvador Estudio de la anatomia y patogenia de un caso de deformidad de Madelung *Revista Medica de Barcelona*, 4, 251-274, September, 1925 (1 case)

- ¹¹⁴ MacLennan, Alex Report of a Case of Madelung's Deformity *British Medical Journal*, 2, 759-760, 1909 (1 case)
- ¹¹⁵ Madelung Die spontane Subluxation der Hand nach vorne *Verhandlungen der Deutschen Gesellschaft für Klinische Chirurgie*, 23, 395-412, 1879 (5 cases)
- ¹¹⁶ Magnus, Georg Über Madelung'sche Deformatat *Medizinische Klinik Berlin*, 8, 2069-2070, 1912 (1 case)
- ¹¹⁷ Malfuson, Daniel Déformation du poignet d'origine probablement rachitique *These de Paris*, July 28, 1894 (2 cases)
- ¹¹⁸ Malgaigne, J F *Traite des fractures et des Luxations* Paris, 2, 711-712, 1855 (1 case)
- ¹¹⁹ Marsan, Felix Sur un nouveau cas de maladie de Madelung *Archives Générales de Chirurgie*, 2, 472-482, November, 1908 (1 case)
- ¹²⁰ Marsan, Felix La Maladie de Madelung (Radius Curvus) *Gazette des Hôpitaux*, 81, 1671-1679, 1909 (No new reports, but an excellent discussion and bibliography up to 1909)
- ¹²¹ Masmonteil, Fernand À propos de la pathogenie de la maladie de Madelung (Radius Brevior) *Gazette des Hôpitaux*, 93, 101-103, 1920 (Traumatic deformity)
- ¹²² Masmonteil, Fernand Toujours à propos de la pathogenie de la maladie de Madelung *Lyon Chirurgical*, 18, 351-355, 1921 (1 case)
- ¹²³ Massabauu, Soulas et Nichet La Maladie de Madelung *Archives de la Soc Méd et Biol de Montpelier*, 15, 191-195, May, 1934 (1 case)
- ¹²⁴ Mathieu, Ch, et Joseph, V Radius Curvus Bilateral *Societe Med de Nancy*, May 24, 1922, *Revue Medicale de l'est*, 1, 586, 1922 (Same case ref 145)
- ¹²⁵ Mathieu, Ch, et Joseph, V À propos d'un cas de Maladie de Dupuytren-Madelung bilaterale *Revue Medicale de l'est*, 1, 691-701, 1922 (2 cases)
- ¹²⁶ Mauclore Discussion on Finzi's⁸⁵ paper, Seventeenth International Congress of Medicine, London, 1913, 7, Part 2, Orthopedics, p 344
- ¹²⁷ Mauclore Trois observations de subluxation progressive du poignet *Comptes rendus de la Soc de Chir de Paris*, February 9, 1916, *Bulletins et Memoires de la Société de Chirurgie de Paris*, 42, 344, 1916 (3 cases)
- ¹²⁸ Mauclore À propos du radius curvus *Société de Chirurgie de Paris*, February 11, 1925, *Presse Médicale*, 33, 223, 1925 (Brief mention of the 3 cases reported above¹²⁷)
- ¹²⁹ Mauclore et Labadie-Lagrave Un cas de Maladie de Madelung *Bull et Mém de la Soc de Chirurgie de Paris*, 35, 695-596, 1906 (1 case)
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INTRACAPSULAR FRACTURES OF THE NECK OF THE FEMUR*

A STUDY OF ONE HUNDRED NINETY CASES

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EVALUATION of any method of treatment of intracapsular fractures of the femoral neck is exceedingly difficult because of the varied and contradictory reports of end-results found in the literature.

For the past 20 years the Whitman¹ abduction treatment has been the most popular and widely employed method for the treatment of fractures of the hip. Although other methods, including open operation, have been used in a few clinics, it was not until 1931, when Smith-Petersen² presented his work on internal fixation, that operative procedures became widely utilized. This widespread acceptance of a new surgical approach to the problem would indicate that the closed methods previously used had proved unsatisfactory.

In 1930, a commission appointed by the American Orthopedic Association³ investigated the end-results of the Whitman method of treatment of intracapsular fractures, and in a careful study of 210 cases, throughout the country, found that osseous union was obtained in 53.8 per cent of the cases. In 1934, McAusland⁴ reported a series of 60 cases treated by the Whitman method in which 58.3 per cent obtained bony union. In the same year Henderson⁵ reported that 66.6 per cent of a series of 36 cases treated by the Whitman method resulted in bony union. Howard and Christophe,⁶ in 1934, reported 70 per cent bony union in 43 cases treated by the Whitman method. As late as 1936, Whitman⁷ stated that the lowest percentage of bony union reported in the series of cases treated by his method was 58 and the highest 90. In the same year Mensor and Dewey⁸ reported 50 cases admitted to the Languna Honda Home, in which nonunion resulted in every case. Only five of these cases received primary treatment in this hospital. In 1937, Kleinberg reported a series of 12 cases, treated by a modification of the Whitman method, in which ten, or 83 per cent, were firmly united within two to three months.

In an attempt to determine the reasons for this wide discrepancy, we find several factors which influence the interpretation of the end-results.

(1) The Length of Follow-Up.—Since healing is admittedly slow, and late complications often result, reports based upon a follow-up of two or three months are not comparable to reports of cases followed for one or two years.

(2) Differentiation as to Location and Type of Fracture.—Campbell⁹ has pointed out the failure of many authors to differentiate clearly between intertrochanteric and intracapsular fractures, and between impacted and unimpacted

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intracapsular fractures He¹⁰ has shown that more than 50 per cent of all fractures of the hip are intertrochanteric or impacted Failure to recognize the variation in prognosis in these various groups leads to confusion in comparing end-results Magnuson¹¹ and Smith-Petersen¹⁶ have also emphasized the fact that subcapital fractures, impacted in a valgus position, invariably unite irrespective of the method of treatment employed

(3) Differentiation Between Recent and Old Fractures —A report based upon all fractures admitted to a large hospital, regardless of where the primary treatment was received, will of course include many ununited fractures transferred from other institutions or admitted for a reconstruction operation, and will, therefore, result in a high percentage of nonunion

(4) Statistical Variations —It is obvious that statistical reports will vary with the author's choice of cases In comparing end-result statistics it is necessary to know whether the percentage is computed from all cases, including unknown and fatal cases, or from only living, followed-up patients

In an attempt to determine the results of closed methods of treatment of intracapsular fractures admitted to two hospitals, a study was made of 190 consecutive cases from the New York Hospital over a 20 year period (1915–1935), and from the St Vincent's Hospital over a ten-year period (1925–1935) Although 190 patients were admitted to these hospitals during the years mentioned, 34 of them were admitted one month or longer after injury, having had previous treatment Some were admitted for reconstruction operations for nonunion or were treated for some other unassociated illness

In estimating end-results of the closed methods of treatment, only those cases that received primary treatment in the above hospitals are included No cases of intertrochanteric fracture are included in this report The patients were treated by 31 surgeons

TABLE I
SEX AND AGE INCIDENCE IN 190 CASES OF
INTRACAPSULAR FRACTURES OF NECK OF FEMUR

<i>Sex</i>	
Females	135 cases—71%
Males	55 cases—29%
<i>Age</i>	
Average age	60
Youngest	12
Oldest	95
Cases receiving primary treatment	156
Cases receiving primary treatment elsewhere	34

Sex and Age Incidence —There were 135 females (71 per cent) and 55 males (29 per cent) in the entire series The average age was 60, the oldest being 95 and the youngest 12 (Table I)

TABLE II

MORTALITY RATE AND CAUSES OF DEATH

156 Cases Average Age, 72 27 Deaths—Mortality, 17.3%

Pneumonia	8 cases
Pulmonary embolism	8 cases
Cardiac failure	5 cases
Multiple injuries	2 cases
Sepsis (from decubitis)	2 cases
Chronic nephritis	1 case
Intestinal obstruction	1 case

Mortality—There were 27 deaths, a mortality of 17.3 per cent. It is significant to note that the average age of the fatal cases was 72, 24 of the 27 cases being over 60 years of age. The average duration of treatment before death was 40 days.

A study of the causes of death shows that pneumonia and pulmonary embolism account for over half of the fatalities (Table II). This finding closely parallels the statistics of Howard and Christophe.⁶

In four of the eight cases dying of pulmonary embolism autopsies were performed. In the remaining four the clinical diagnosis seemed justifiable, but no autopsy was done. The high mortality due to pulmonary embolism suggested further study to determine whether prophylaxis or treatment could minimize this complication. The average age of these patients was 70. The average duration of treatment before death was 17 days, the shortest being seven, and the longest 39 days. The form of treatment of the fracture did not seem to bear any relation to these deaths except that all of the patients were bedridden. Four of these cases were treated by the Whitman method and could be turned in bed frequently. Although there was a fairly large number of cases in the entire series in which phlebitis was reported as a complication, in only one of the fatal cases of embolism was this complication recorded.

In view of the high mortality due to pulmonary emboli, it may be of value to consider clotting factors and prophylactic treatment as outlined by Bancroft and Stanley-Brown.¹² The high incidence of pulmonary emboli is also a definite argument in favor of that form of treatment which permits of mobilization and short periods of bed confinement.

TABLE III

RESULTS IN 34 PREVIOUSLY TREATED CASES

Deaths	1
Nonunion	23
Union	2
Unfollowed	8

Results of Treatment—The results of cases admitted to the Hospital four weeks or longer after injury are shown in Table III. Of the 23 cases of nonunion, 18 were old cases with frank nonunion at the time of admission. Thirteen of these cases were admitted for, and subjected to, reconstruction.

operations, bone-pegging or arthrodesis. The two cases resulting in union were complete midcervical fractures. Both had been treated at home by bed rest only, one for 42 days, and the other for 46 days before coming to the hospital. After admission they were treated by the Whitman abduction method, and both united with absorption of the neck and a coxa vara deformity (Figs 12 and 13)

TABLE IV
FOLLOW-UP RESULT IN 156 RECENT FRACTURES

Deaths (in hospital)	27
Deaths (within one year of discharge)	5
Unfollowed	55
Living cases followed one year	69

CLINICAL RESULTS OF 69 FOLLOWED CASES			
Satisfactory	22	31	9%
Unsatisfactory	47	68	1%

Follow-Up Results —The follow-up results of the series of 156 recent fractures are shown in Table IV. There were 32 cases known to have died in the hospital or within one year of discharge. Of the remaining 124 cases, 55 were unfollowed, and 69 were reported upon one year or longer after injury. Of these, 46 had had an examination and roentgenograms one year or longer after admission to the hospital and 23 reported by letter. No attempt was made to grade the results as good, fair or bad, in the cases reporting by letter because the information given was too meager to arrive at accurate conclusions. Those cases known to have bony union with good function and those cases reporting stable weight bearing hips, who returned to former occupations, are considered satisfactory. Those cases known to have nonunion with poor function, and those reporting a disability necessitating support in walking, are considered unsatisfactory.

TABLE V
STATISTICS RELATIVE TO RESULTING BONY OR NONUNION IN 46 FOLLOWED CASES

Bony union	8 cases—17.5%
Nonunion	38 cases—82.5%

METHODS OF TREATMENT IN 46 FOLLOWED CASES

Procedure	No of Cases	Nonunion	Bony Union	Percentage of Union
Whitman	35	30	5	14.2
Traction	9	7	2	22
Sandbags	2	1	1	50

Bony Union —In determining the presence or absence of bony union, only those cases are included in which roentgenologic examination was available one year or longer following the date of injury. Of the entire series of 129 living cases only 46 were examined physically and had roentgenograms taken after

this period of time. This is a low follow-up percentage and illustrates one of the difficulties in compiling an accurate report in such cases. Many are transferred to other hospitals during the immobilization period, many die during the first or second year after the injury and others are totally disabled and cannot return for physical or roentgenologic examination.

Table V shows the results in the living cases followed and examined roentgenologically one year or longer after injury. There are 46 followed cases of which eight, or 17.5, per cent resulted in bony union, while 38, or 82.5 per cent, resulted in nonunion.

Of the 35 cases treated by the Whitman method only five cases (14.2 per cent) obtained a bony union. Of the five successful cases, one was incomplete and three were impacted. Only one of the successful cases was a complete unimpacted fracture.

Adherents of the Whitman method have stated that such poor results indicate that the surgeons did not use the method properly. It seems logical to assume that if, after 30 years of general use, a method is successful only in the hands of a limited number, it should not be advocated as a general method of treatment.

This record of poor results is made more discouraging after a study of the cases which united (Table VI).

TABLE VI
EIGHT CASES OF BONY UNION

Type of Fracture	No of Cases	Treatment	Clinical Result
Incomplete	1	Whitman	Aseptic necrosis (Whitman reconstruction)
Impacted in valgus	5	Whitman, 3 Traction, 1 Sandbags, 1	Good
Unimpacted, complete	2	Whitman, 1 Russell traction, 1	Good

Of the eight cases resulting in bony union, only two were complete, unimpacted, intracapsular fractures, the remaining six being incomplete or subcapital fractures impacted in the valgus position.

Nonunion—In studying the cases of nonunion it was found that, invariably there was absorption of the neck with more or less upward displacement of the femoral shaft. In some cases the absorption involved not only the neck but also the femoral head. In some cases evidence of nonunion appeared in less than three months but in many instances definite evidence of nonunion was not apparent until after three months. In other cases union was apparently solid, as determined by roentgenologic examination six and nine months following the injury, nonunion being demonstrated thereafter. Upward displacement of the femoral shaft increased after weight bearing was attempted, and in most cases shortening of one or two inches resulted.

Four of the ununited fractures treated by the Whitman method appeared

INTRACAPSULAR FRACTURE OF FEMUR

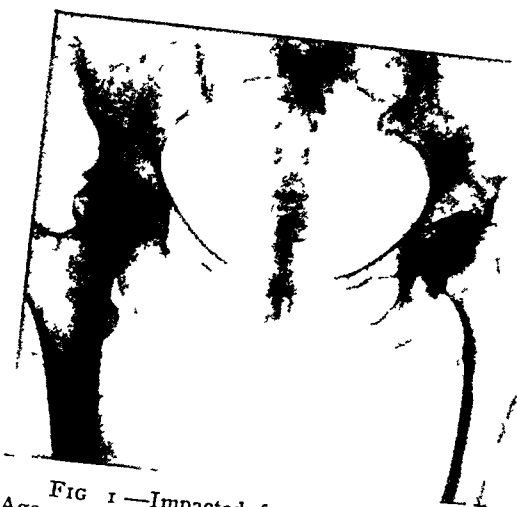


FIG 1—Impacted fracture in valgus, right
Age 32 Whitman treatment Union Roent
genogram five years after injury

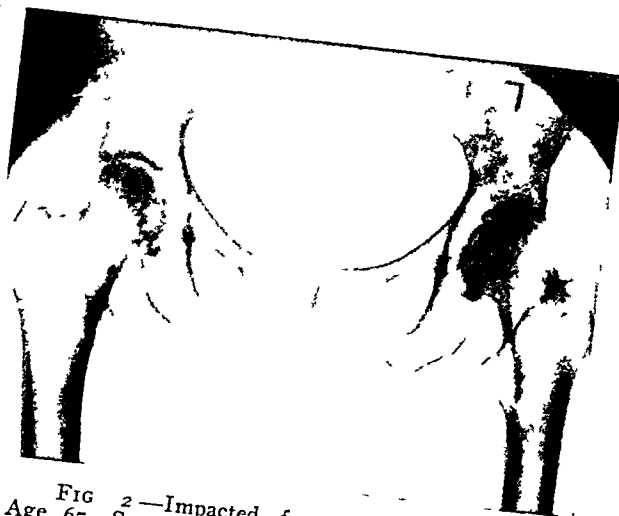


FIG 2—Impacted fracture in valgus, right
Age 67 Sand bag treatment Union Roentgen
ogram three years after injury



FIG 3—Impacted fracture in valgus, right
Age 30 Whitman treatment Union Roent
genogram ten and one half years after injury



FIG 4—Impacted fracture in valgus, left
Age 50 Whitman treatment Union Roentgen
ogram seven and one half years after injury

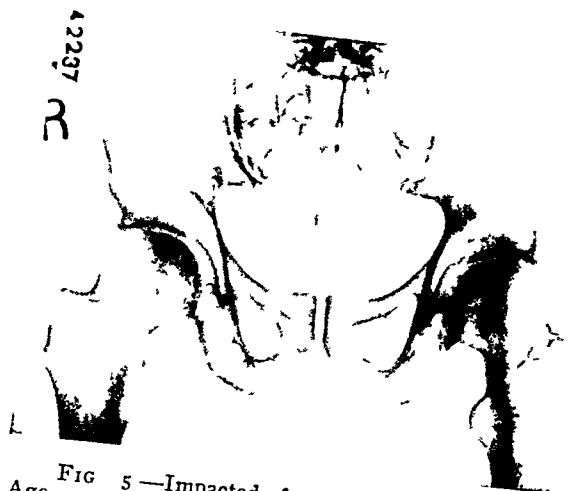


FIG 5—Impacted fracture in valgus, left
Age 37 Russell traction Union Roentgeno
gram 14 months after injury



FIG 6—Incomplete fracture, left Age 16
Whitman abduction spica Roentgenogram at
time of injury

impacted in the original roentgenograms. None of these had lateral views made. All of the remaining cases were complete, unimpacted fractures, most of them with displacement and rotation apparent in the roentgenogram.

Those cases treated in the past few years, since the use of lateral roentgenograms, showed no improvement in results. Many were apparently perfectly reduced in both the anteroposterior and lateral views, yet none of the complete midcervical fractures having the benefit of lateral roentgenograms united.

Eight of 38 cases of nonunion were subjected to operative procedures. Four had Whitman reconstruction operations, one being a failure, the other three were successful. In two cases a Brackett operation was performed, one was successful and one unsuccessful. In one case a bone peg was used with an unsuccessful outcome, and in one case an ostotomy was performed, the result being unknown.

Of the 30 remaining cases, two were able to walk without support and with little pain or limitation of motion, after three years. Both had marked limps but were able to carry on their occupations. Four were able to walk with the aid of a cane, but their locomotion was definitely limited. All of these patients were totally disabled for two or three years. Ten were totally disabled and practically bedridden after a period of three years. The remaining 14 were not followed long enough to estimate function.

Cases Resulting in Union—In the followed cases there were five in which the original roentgenograms showed impacted, subcapital fractures with the head in the valgus position. All of these cases united with excellent anatomic, as well as functional results. Roentgenograms, as shown in Figs 1, 2, 3, 4, and 5, showed healing with negligible absorption of the neck or deformity of the head except for the valgus position. Three were treated in the Whitman abduction spica, one by a Buck's extension and one by sandbags.

There was only one incomplete fracture in the series (Fig 6), a boy of 16, immobilized in a Whitman spica for eight weeks. Roentgenograms at regular intervals showed bony union up to one year. Thereafter, the head showed beginning aseptic necrosis, and at the end of three years the process was well advanced in the head and neck with narrowing of the joint space (Fig 7). Because of pain and disability a Whitman reconstruction operation was recently performed.

This case illustrates the necessity of long follow-up study before end-results may be accurately compiled. It also clearly illustrates that, in injuries to the femoral neck and head, a process of bone absorption, or aseptic necrosis, may result without a complete fracture. There is much emphasis in the literature upon accurate apposition and adequate fixation as necessary factors in the prevention of nonunion, but in the above case these requirements were necessarily fulfilled. The incomplete fracture united. Nevertheless, aseptic necrosis developed. The cause of late changes in the femoral neck and head is not known, but undoubtedly it has to do with injury to the cartilage of the head and to disturbance of blood supply of the head and neck. Speed¹³ has emphasized the fact that this process of absorption may proceed in spite of

INTRACAPSULAR FRACTURE OF FEMUR



FIG 7—Roentgenogram after three years
Fracture united Aseptic necrosis of the
head



FIG 8—Roentgenogram after reduction of disloc-
tion of right hip



FIG 9—Roentgenogram after three years showing asep-
tic necrosis of the head and neck



FIG 10—Unimpacted fracture Age
70 Russell traction Union Roentgeno-
gram two years after injury

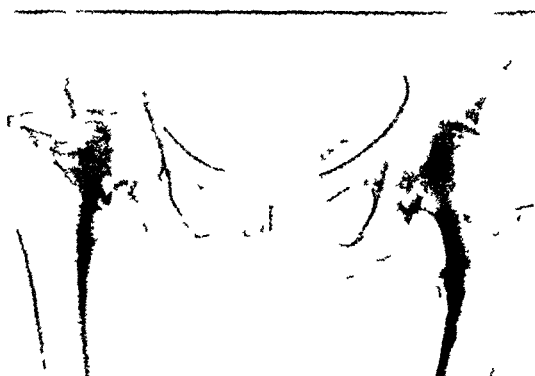


FIG 11—Unimpacted fracture right Age
56 Whitman treatment Union Roentgenogram
two and one half years after injury



FIG 12—Unimpacted fracture left Age
60 Admitted 42 days after injury Whitman
treatment Union Roentgenogram 15 months
after injury

accurate fixation of femoral neck fractures. The same process may follow dislocation of the hip without fracture of the femoral head or neck. Figure 8 shows a roentgenogram of a right hip after closed reduction of a traumatic dislocation. There was a fracture of the rim of the acetabulum. After three years, symptoms of pain and shortening occurred and a roentgenogram (Fig 9), revealed aseptic necrosis of the head and neck. From a study of these cases it is evident that a process of absorption of the neck or head may occur when the problems of proper reduction and immobilization are eliminated. This fact may explain the frequent occurrence of nonunion in midcervical fractures.

Only four complete midcervical fractures were found to have united in the entire series, two being fresh fractures. One was treated by Russell traction, because the age (70) and general condition of the patient contraindicated more radical treatment. Figure 10 shows the roentgenogram of this case, two years after injury with definite bony union and no apparent shortening of the neck. The other recent case was treated by the Whitman method and the result, Fig 11, two and one-half years after injury, shows bony union with absorption of the neck and a coxa vara deformity. The functional result in this case is very good. The remaining two midcervical fractures were admitted for Whitman treatment 42 and 46 days, respectively, after injury. Both united with absorption of the neck and a coxa vara deformity (Figs 12 and 13), but with good function.

In practically all midcervical fractures of the neck of the femur, absorption of the neck occurred and union rarely resulted. The results of the cases shown in Figs 11, 12, and 13 are unusual in this series. In spite of absorption of the neck, the head has united to the shaft. These results are similar to that obtained by Magnuson¹⁴ in his adaptation of the Brackett operation to fresh complete fractures (Fig 14). In this operation a portion of the neck which usually absorbs is sacrificed in reforming the upper end of the fractured neck to be inserted into the hollowed-out head. The greater trochanter is transplanted to a lower position on the shaft. Although this operation is a formidable one, and is applicable only to those patients in fairly good condition, the theory of the procedure is sound, and Magnuson¹¹ has reported satisfactory results.

Investigation of the complete intracapsular fractures in this series of cases would indicate that closed methods of treatment are still inadequate.

With modern internal fixation^{2, 17} these elderly patients are able to be out of bed and may bear weight on the affected leg even before union can occur. These methods are a marked improvement over closed methods of treatment in this respect. Smith-Petersen states that the nail, in itself, does not promote union but allows early mobilization with firm fixation. The method has not been employed over a long enough period to establish the end-results in respect to bony union, but even if late reports indicate a low percentage of bony union, the internal fixation is still an improvement over the closed methods.

Since absorption of the neck with nonunion is the usual result in unim-

pacted intracapsular fractures, it seems that exponents of the early reconstruction operations have evidence upon which to base their plan of treatment. In these cases, if operative procedure may be safely performed, it seems wise to accept inevitable nonunion and to undertake early operative procedures for reconstruction, such as the Magnuson-Brackett¹⁴ operation, or the Schanz osteotomy as described by Schumm¹⁵



FIG 13—Unimpacted fracture, left
Age 39 Admitted 46 days after injury
Whitman treatment Union Roentgeno-
gram 15 months after injury



FIG 14—Brackett operation for
fresh, complete, unimpacted fracture
(from Magnuson) Roentgenogram two
years after operation

CONCLUSIONS

(1) Accurate end-results of any method of treatment should differentiate between (1) Intracapsular and intertrochanteric fractures, and (2) impacted and unimpacted fractures

(2) Accurate end-results of treatment with respect to bony union cannot be obtained without at least one year follow-up roentgenologic examination

(3) Accurate end-results concerning function cannot be obtained under one or two years because (1) Some cases resulting in bony union may develop aseptic necrosis of the head and neck, and (2) some cases resulting in nonunion have a fairly satisfactory functional result

(4) In this series, subcapital fractures impacted in the valgus position, united with little or no deformity of head or neck, regardless of the types of treatment

(5) Complete unimpacted fractures usually result in nonunion with absorption of the neck

(6) Absorption of neck and head may develop even with apposition of fragments and proper immobilization

(7) In this series of cases the Whitman method has shown too few satisfactory results to justify its continued use

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DISCUSSION—DR JAMES M HITZROT (New York) was greatly interested in hearing a discussion on what Kellogg Speed has called "the unsolved fracture," and what Cotton has recently described as the fracture for which the best procedure has not yet been discovered, namely, intracapsular fracture of the neck of the femur. The essential result desired is a satisfactory weight-bearing leg, without pain, and with sufficient motion at the hip joint to allow the patient to sit down with comfort. A great many methods have been devised and are at present being employed to accomplish this result. Just how satisfactory many of them are is a matter open for discussion.

Doctor Hitzrot considered intracapsular fracture of the neck of the femur as occurring in three age-groups. The first is in young people, before the epiphysis of the head of the femur has united to the shaft, the second, in patients between the ages of 20 and 50, and the third, in patients of 50 years of age or more. The problems of treatment are a little different for each

group In the first group, fractures of the neck of the femur or epiphyseal separations require complete, early reduction, and unless this is obtained satisfactorily by manipulation these cases should be operated upon early and the replacement obtained by actual exposure of the fracture line, every attempt being made to conserve the growing portion of the bone In the second group, reduction by open operation or by fixation with various forms of metal nails, screws, etc., is probably the method of selection, and, in Doctor Hitzrot's opinion, the future will see more operative procedures in this group than at present In the group over age 50, and especially in the older members of this group, the primary essential of treatment is the general care of the patient because most fatalities occur in this group Naturally, any series of cases from age 60 upward, will show the highest mortality, and in these elderly people that type of treatment must be instituted which will give them the most comfort and run the least risk of endangering their lives The incident of nonunion in patients more than 50 years of age, is highest Therefore, the results in this group are as yet not satisfactory in that, after a long period of treatment, these patients usually have an unsatisfactory weight-bearing hip This occurs no matter what the original treatment may have been, since the etiologic factors and cause of the nonunion are not controlled by any of the operative procedures That the newer methods of fixation by nails, screws, etc., are a more comfortable treatment, allow these patients more freedom, and are less confining, can generally be accepted, but the late results are not as yet proven to be more satisfactory than those of the earlier manipulative methods If nonunion occurs due to absorption along the fracture line the same failure to obtain a satisfactory weight-bearing leg results

Fractures of the neck of the femur deserve consideration also from another point of view, namely, some type of operative procedure which will avoid the disappointing results and which will enable the patient to be up and about with a weight-bearing leg and a minimum amount, if not an entire absence, of pain on walking

Doctor Hitzrot felt that, in properly selected cases, some type of reconstruction operation performed early would give the patient a more satisfactory weight-bearing leg than could be obtained by any form of treatment which attempted to obtain union along the fracture line In a discussion with Doctor Magnusson, Doctor Hitzrot understood him to be of the opinion that the Brackett operation, performed early, would produce this result Even if union does not occur following this operation, the weight-thrust will give the patient a satisfactory weight-bearing leg without pain, and the patient will be able to get about earlier than if operation were undertaken after nonunion has occurred

Doctor Hitzrot emphasized that an operation, of the type described by Whitman, the so-called "Whitman reconstruction" operation, must also be given consideration If this is undertaken early, the resulting weight-bearing leg is much more satisfactory than if it is performed late Doctor Hitzrot's experience with 20 cases, in which this procedure was carried out, after it was definitely established that nonunion was occurring, demonstrated satisfactory results in 18 instances, which led him to the conclusion that if the operation had been performed early the result would have saved the patient a good deal of trouble His experience with other types of procedure or the results which he has seen have not seemed entirely satisfactory His results with the Brackett operation have not been quite as satisfactory as those obtained by Doctor Magnusson This, he thought, might be due to

a fault in his operative technic, in that he did not get the head fragment so fixed that the weight-thrust was directly upward through the shaft, and when the weight-thrust becomes exerted at an angle as the result of this operation the end-results are likely to be disappointing

Neither of these operations is a minor undertaking, and the cases upon which they are performed should be carefully selected. If the patient is properly prepared, Doctor Hitzrot's experience with the Whitman reconstruction operation has been such that in his opinion many of these patients will stand one of these operative procedures without any great difficulty. Just what the mortality will be in these cases is problematic. The cases upon which Doctor Hitzrot had operated late have, up to the present, all been carefully prepared and selected for the operation. Among these he, fortunately, has not had a fatality. If this care in selection is not made, naturally the mortality will be greater.

Doctor Hitzrot's experience with the various types of bone grafting in these fractures, which he began to employ as early as 1912, using autogenous and beef-bone dowels and screws, had not given satisfaction, and when healing occurred in the early cases it seemed that it would have occurred equally as well without the operation. There is nothing about the bone graft that will alter the process which tends to produce absorption along the neck, even in young individuals, and the fixation obtained by these various types of graft has not been as firm as that which can be obtained by various types of metal nails and screws, and is, in addition, much more difficult of accomplishment.

Although reconstruction operations leave the patient with a shortened leg, they do not result in much more shortening than occurs when the neck bends later, nor do they give as much shortening as occurs after the absorption has taken place on the shaft side of the neck. The early application of weight to the reconstructed neck prevents, to a large degree, this absorption, and Doctor Hitzrot was convinced that some such radical procedure as the Brackett operation or the Whitman reconstruction operation must be given due consideration in the treatment of these unsolved fractures. Just what procedure will give the best result will have to await the results obtained by many well equipped surgeons, and to obtain a true perspective on these results, the cases should be followed for at least two years or longer after injury before arriving at any conclusion as to the desirability of either procedure.

DR DONALD GORDON (New York) reviewed Doctor Wade's statistics in seven series of end-results for the Whitman method, which varied from 53 to 83 per cent satisfactory. If the figures of Whitman are excluded, the average of successful results was 55 per cent, including Mensor and Dewey's statistics of 50 cases with zero success. If that group is left out, the average becomes 66.2 per cent, which compares favorably with recent reports of nearly 70 per cent in series analyzed by other men. Mensor and Dewey's figures depart so far from the major cross-section of the results quoted by Doctor Wade, that it would appear that the surgeons made such a poor application of the Whitman method that it is questionable if they would have done any better by employing a more complicated procedure.

Concerning Doctor Wade's statement with regard to the group he studied—that "It seems logical to assume that if after 30 years of general use a method is successful only in the hands of a limited number, it should not be advocated as a general method of treatment"—Doctor Gordon said that the statistics shown by Doctor Wade for the two New York hospitals certainly reflected little credit on the method or the hospitals, as compared with those quoted by men from other cities, the general reports of success with the Whitman method.

as to end-results, whether functional or with bony union, being at variance with the figures shown in Doctor Wade's study. This study did not reveal any data to suggest a technic which would afford any better results in the hands of those unable to use the Whitman or closed methods with an average degree of success. Doctor Gordon was not convinced from the data presented that closed methods of treatment should be given up. Human judgment suffers a severe strain in choosing which method of procedure to employ where a study of Table V, presented by Doctor Wade, reveals that two cases treated with sandbags gave a 50 per cent incidence of bony union in the series of cases critically examined by Doctor Wade.

Discussing the ingenious and specialized technic presented by Doctor Bergamini and Doctor Dooley, Doctor Gordon thought that their own, combined with other standard procedures, involved the introduction of a pin of Vitallium with a shearing resistance up to 24,000 pounds, or 12 tons, and said that such a pin should resist corrosion. Its prolonged tolerance by the tissues of various patients will have to be learned. Its strength should support weight-bearing of even the very obese, until the fracture has had an opportunity to unite, if it will, or for a longer period if it will not.

The method of finding the angles formed by the axis of the neck and shaft from the tracing is simple and useful, but it would be of help if the authors would state what corrections should be made when the upper end of the femur is not a normal one, because of former pathology. The control of the direction of the pin appears to be within the safety limits required. Doctor Gordon wondered if the authors had had any pins deviate enough to cause a complication.

Doctor Gordon stated that the Leadbetter¹ method of reduction stood alone in reducing and proving reduction before being controlled roentgenographically. He felt that the technic of the lateral view of the normal or injured hip, as shown by Doctor Bergamini, was most novel and should be helpful for other purposes in this region as well as for localizing foreign bodies other than the pin. The determination of the precise position of the injured or well leg by the use of the inclinometer would be precluded where a stiff knee or mid-thigh amputation existed in either leg, and, therefore, a simpler technic would be necessary.

Only one stage in the development of the technic for the introduction of flanged pins in treating a fracture of the neck of the femur was presented. Conclusions were furnished based upon the authors' extensive personal experience, which Doctor Gordon found it difficult to agree with completely, mainly on the basis of his lack of similar experience with an entirely new procedure, and in the absence of any data on their results. The time allotted for the presentation, of course, did not permit the presentation of these data, without it one would not be in a position to apply the yardstick of the results of similar pinning procedures or to pass judgment on its comparative value. Certainly the attention to the many details which appear to furnish precise methods in each step, leaving little to fallacious judgment, would appear to render a better operative result and afford the surgeon the satisfaction of precision which should eliminate one of his worries.

Doctor Gordon doubted whether the skillful technical minds of the authors would remain satisfied even with the present technic, and believed that they would simplify it in the future. The procedure appears to give a great degree of accuracy in locating where the pin is to be placed and in directing its course, but the authors, while assuring that the procedure is simple, do not mention how many hours must be spent on the development of an organization, in

order to enable one to carry out the method simply. This encouragement is needed to induce a trial of any method, but it is only too obvious that anyone attempting the procedure presented, without first-hand experience with those who have developed it to its present degree of perfection, would find many pitfalls. It is the early errors, produced by the pitfalls resulting from inexperience, which tend to detract from the merits of a technic in its early life, and to obscure its true value in the late results. A report in the future by the authors of their complications, sequelae and three-year results based on present standards will be of great value in determining and preserving the good points of their technic. In the main problem, when any pin or internal retention device has been placed in a reduced fracture, any technic must be submitted to the many as yet unknown factors of physiology and pathology and the limited life expectancy in cases of this "unsolved" problem.

Doctor Gordon said that, although inexperienced in pin work, he personally believed that in the hands of a properly trained organization it affords accurate reposition. A small, strong, noncorrosive pin should cause a minimum of damage in the open operation which such work requires. Doctor Bergamini's and Doctor Dooley's method appealed to the speaker as a step forward in pinning technic which, by early mobilization of the patient to the upright position and by improving the blood supply of the femoral neck, will do much toward bringing about a union and minimizing the subsequent bone absorption.

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DR PAUL K SAUER (New York) Without minimizing in the slightest the credit due Doctor Whitman, it must nevertheless be admitted, as has been so well demonstrated by Doctor Wade, that the Whitman method except possibly in the hands of a select few has not proved adequate in the treatment of intracapsular fractures of the neck of the femur.

During the past six years, at the City Hospital, Doctor Sauer had remarked the continued readmission of fracture of the hip cases year after year, which gave rise to the suspicion that their method of treating intracapsular fractures of the femoral neck left much to be desired. Their impression of the poor results was not only substantiated, but upon analysis of the cases from 1929 to 1936, it was ascertained that the actual results were even less favorable than they had suspected.

In Doctor Sauer's opinion no result that is less than two years old should be considered, much less reported, as a careful follow-up of results at the end of two or more years often dispels the impression of a bony union, which had seemed a successful accomplishment at the end of nine months or a year.

During the seven years up to January, 1936, there were 96 cases of intracapsular fractures of the neck of the femur treated at the City Hospital (No cases of intertrochanteric fractures are here included). It was noted that although several cases were reported by the roentgenologist as being impacted when they were first examined roentgenologically, not a single case of impaction was found on later examination.

An analysis of the 96 cases showed the sex incidence to be 63 females and 33 males, a ratio of approximately 2:1. The average age of all the patients was 62.5 years, the youngest 26, and the oldest 95. The mortality rate was 25 per cent.

INTRACAPSULAR FRACTURE OF FEMUR

TABLE I

ANALYSIS OF 96 CASES OF INTRACAPSULAR FRACTURE OF THE NECK OF THE FEMUR

Total number of cases	96
Average age	62.5
Youngest	26
Oldest	95
Average morbidity	5.3 mos
Mortality	25%
Cases receiving more than one method of treatment, other than reconstruction operation	27 (35%)
Number of cases of bony union	0
Number of cases receiving reconstruction operations	19 (20%)

Table II shows the various methods of treatment instituted. A justifiable question would be how many of these cases were properly reduced in the first place before the application of the Whitman spica, and in how many of those properly reduced was the reduction maintained after the application of the spica? I don't know, but I assume just about as many as are usually reduced and maintained in the average hospital. You will also notice in Table II that the only case in which bony union was obtained, was complicated by a simultaneous intertrochanteric fracture in which a long upper fragment was wired to the shaft. Otherwise the record of bony union is 100 per cent nil. Twenty-seven, or 35 per cent, of these cases received more than one method of treatment and still there was no bony union obtained.

TABLE II

ANALYSIS SHOWING METHODS OF TREATMENT EMPLOYED AND RESULTS

Methods of Treatment Employed	No	Average Age	Age of Youngest	Age of Oldest	Average Morbidity	Mortality	Mortality Per Cent	Union	No of Cases Receiving Other Treatment
Unknown	4	59	43	76	Unknown	1	25	0	0
Russell traction	6	58	34	76	1 mo	0	0	0	5 (83%)
Whitman spica	58	63.5	26	86	4.8 mos	8	14	0	15 (21%)
Bozsán drilling, with spica	8	65	54	79	4.9 mos	1	12.5	0	4 (50%)
Bozsán drilling, Roger Anderson	1	34	34	34	3 mos	0	0	0	0
No treatment, sandbags	12	69	53	95	19 mos	6	50	0	1 (8%)
Roger Anderson, wiring shaft	1	45	45	45	7.5 mos	0	0	1*	0
Kirschner wire, pinning	3	63	56	70	5 mos	1	33	0	1 (33%)
Jones splint, bone graft	1	42	42	42	9 mos	0	0	0	1 (100%)
Thomas splint, walking caliper	2	65.5	55	76	1.5 mos	1	50	0	0
Smith-Petersen nail	1	40	40	40	5 mos	0	0	0	0
Moore nail	1	76	76	76	1.5 mos	1	100	0	0
Wire nail	1	26	26	26	5 mos	0	0	0	0
Buck's extension	1	67	67	67	2 mos	0	0	0	0

* Bony union obtained, fracture complicated however by an intertrochanteric fracture which was wired.

Based on the findings of our analysis of these cases it was decided that we were most unsuccessful in reestablishing these people as an economic asset to the community, and that our usual method of treating these cases was faulty. It seemed that if nonunion was to be the rule in these cases when treated by

the ordinary methods, some other type of therapy had to be instituted. Therefore, it appeared that some type of reconstruction operation as the primary treatment was indicated in order to obtain an early satisfactory result.

TABLE III

ANALYSIS OF THE 19 CASES WHICH RECEIVED RECONSTRUCTION OPERATIONS

Number of cases having reconstruction operations	19
Average age	43 3
Youngest	28
Oldest	76
Number having had previous treatments	18
Average morbidity before reconstruction	7 mos
Average morbidity after reconstruction operation	4½ mos
Mortality (4 cases)	21%
Results	
Good	11
Fair	1
Failure	3

TABLE IV

ANALYSIS OF THE TYPES OF RECONSTRUCTION OPERATIONS EMPLOYED AND RESULTS

Types of Reconstruction Operations	No	Average Age	Age of Youngest	Age of Oldest	No Pre-viously Treated	Average Morbidity before Reconst	Average Morbidity after Reconst	Mortality	Mortality Per Cent	Results
Whitman reconstruction	3	56 3	52	64	3	10 mos	7 mos	2	66 6	1 walking
Brackett operation	1	28	28	28	1	3 mos	5 mos	0	0	Ankylosis walking
Lorenz bifurcation	15	60 6	39	76	14	7 7 mos	4½ mos	2	13 3	9 good 1 fair 3 failures

Four types of operation were considered: Whitman reconstruction, Colonna's operation, Brackett's operation, and the Lorenz bifurcation. The first two were discarded because they necessitate opening the hip joint and removing the head of the femur. Frequently these operations lead to ankylosis of the joint. The Brackett operation, while it makes use of the head, demands that the joint be opened, a procedure which is not without the attendant dangers of shock and infection. Therefore, the Lorenz bifurcation was chosen as being the most suitable to be employed at the City Hospital for the following reasons:

(1) The hip joint need not be opened, the operation being an extracapsular osteotomy.

(2) The head of the femur is left in place, and is used as a movable point of support.

(3) There is practically no shock to the operation, and the procedure can be borne by any patient capable of undergoing an operation.

(4) The time of operation is short, 20 minutes being all the time required except for the application of the plaster encasement.

(5) The danger of infection is minimal. If infection does take place, the extracapsular tissues are much more capable of taking care of it than the joint surfaces.

(6) There is very little shortening of the leg. While there is some absolute

shortening, there is relative lengthening due to the abducted position of the leg and the tilt of the pelvis when walking. However, a heavy sole on the shoe of the affected leg will overcome most of the limp.

(7) The mortality is very low. Out of our series of 15 cases there were only two deaths. One patient died of a coronary occlusion ten days after operation, and the other one of a pneumonia two and one-half months post-operative.

There is, to-day, no one satisfactory method of treatment that is applicable in all cases. Many factors, such as the economic and physical status, age, and the conditions under which treatment must be rendered, will of necessity compel different methods of treatment to be instituted.

DR WILLIAM DARRACH (New York) also felt, as had been mentioned by the speaker, that it was a great mistake to draw any conclusions relative to bony union or the vitality of the femoral head during the first two years, and cited three cases illustrating this contention.

The first case was that of a woman, age 72, who had had an open reduction with the introduction of a Smith-Petersen pin. She was walking around at the end of nine weeks. She continued to walk without pain and with almost complete motion until the thirteenth month. At this time while turning over in bed she experienced a sudden severe pain in her hip and was unable to bear her weight on it. Roentgenologic examination showed that the pin had broken and that the fragments had separated. At the end of seven years there was almost complete absorption of the head.

Another case showed bony union nine months after open pinning, with good motion. The pin was removed, and her range of motion gradually decreased and the pain increased. Roentgenologic examination showed marked flattening of the head, notwithstanding the fact that bony union had occurred.

The third case, a woman, age 29, had come up from the South in a plaster spica with an end-to-side position of the fragments. A closed reduction seemed to give good apposition, but after five months it was evident that there was no union and an open reduction was carried out with insertion of a pin. This also failed and a second open reduction and reinsertion of a pin was carried out 11 months later. This resulted in bony union, but after three years the head had become considerably flattened, and at the end of seven years a roentgenogram shows a very misshapen, flattened head. Yet in spite of this there is evidence of a good joint space. She has a marked limp, marked limitation of abduction, internal rotation and flexion, but often spends most of the day on her feet, rides horseback and does not use either a cane or a crutch.

These three cases demonstrate that one cannot always tell at the end of one or even two years, what the results will eventually be. The problem of intracapsular fracture is still "unsolved." With regard to trochanteric fractures, one does not have to worry quite so much. However, a great deal of encouragement may be found because of the marked improvement which has taken place in the treatment of these cases. A few years ago, C. R. Murray made the statement that to get good union one should first get a good reduction, second, maintain that good reduction, and third, get bony union. Doctor Darrach added two other factors: (1) You have to save the patient's life, and (2), you have to protect in some way, if possible, against the late changes that tend to take place, such as flattening out of the head, breaking down or shortening of the neck. These five points must all be borne in mind.

Everybody's mortality has been reduced a great deal—Doctor Darrach said this was true of his because of a number of factors in this special group, one of which he thought was internal fixation. His attitude at first had been that

internal fixation, that is, open reduction with insertion of a Smith-Petersen pin, should be performed in all cases that could withstand such a procedure. However, he now feels that an open reduction and employing a Smith-Petersen pin should be performed only if it is thought the patient will not stand plaster encasement and long bed stay. The pendulum has swung the other way. In older people, open reduction seems safer than to employ a plaster encasement, even though it is a long operation. Doctor Daiiach's mortality had been definitely reduced both by undertaking an open operation, and through better after-care. A great many more lives can be saved if the patient can be enabled to get up sooner. The position on this subject seems to change every two or three years, and it has to do so if anything is to be learned. Doctor Daiiach said he was not certain what is the best method of handling these cases. One series was tried employing the Smith-Petersen procedure, not dividing the glutei, and then another series in which, in order to improve the blood supply, some muscle was transplanted to the head fragment, but the results did not compare favorably with those of some others, especially those reported by Thornton, who has had 60 cases, in which he has obtained most excellent results from blind nailing. Doctor Daiiach said he was now going to start in doing some blind nailing. He did not think, however, that he was up to using the fascinating arrangement described by Doctor Bergamini.

One must keep trying out different methods, studying results, not deceiving one's self, following one's cases through, and actually finding out just what the conditions are at the end of two, three or five years. If all will do this, then, in another 15 or 20 years, it will probably be possible to get somewhere in solving this most difficult but most fascinating problem, namely, fracture of the neck of the femur in the capsule where the blood supply is poor.

DR. FREDERIC W. BANCROFT (New York) said that it had been his good fortune to have heard many talks on fractures of the neck of the femur during the period of three years in which he has been connected with the Committee on Fractures, so that he has a passive knowledge without great actual experience on the subject. On the other hand, he said he was not a strong protagonist of one method or the other, and had formed some theoretic ideas from listening to discussions. He thought everyone would agree that the four steps in the progress of treatment of fractures of the neck of the femur were:

(1) The Whitman method, which produced the first real active principle of abduction in the treatment of fractures of the femur.

(2) The introduction of the lateral roentgenographic view, which showed that the anteroposterior view did not adequately give the position of the fractured ends and showed that a great many femurs treated by abduction had never been properly reduced.

(3) The Leadbetter or some similar method, which presented the actual method of reducing the fragments.

(4) Internal fixation.

Doctor Bancroft was sure, that if he received a fracture of the neck of the femur he would wish first to be in the hands of a man well versed in the treatment of fractures. He was also sure that he would wish some means of internal fixation. He also felt that he should like the method employed by Doctor Thornton, who treats a fracture of the neck of the femur as an immediate emergency operation. If admitted at night the patient is treated as any other emergency would be. This procedure has a very definite advantage. The fracture is reduced with a minimum amount of trauma, before the capsule is distended with fluid, and before the surrounding muscles have become

infiltrated with blood. If the reduction has been delayed for several days, fibrin must have adhered to the ends of the bone, as is seen in cases where open reduction for fracture of the patella is performed, and good approximation cannot be effected between the ends of the bone if they are coated with fibrin as can be accomplished when they are not.

The problem of the type of internal fixation is still to be determined. Doctor Bancroft said his preference would be Moore nails rather than the Smith-Petersen nail, as they seem to give a better fixation of the fragments with less foreign body reaction. The ideal has not been reached because, as Doctor Wade showed, even with internal fixation the neck may become absorbed, resulting in nonunion. In one of the roentgenograms shown, where the bone was presumably being extruded, it seemed to him that the extrusion was the result of the shortening of the neck and not eviction of the nail. If, on the other hand, Doctor Bancroft should not be in a hospital, where immediate operation could be performed, and delayed union resulted, he would like to have a reconstruction operation, probably based on the Brackett procedure. This assumed, he said, that he would be in a hospital with proper facilities for roentgenograms to be taken in the operating room, and with an adequate method for taking a lateral view.

DR ARMITAGE WHITMAN (New York) agreed with almost all of the speakers' statements, and appreciated his very painstaking follow-up of the routine cases as they occurred in two hospitals over a period of 30 years. However, statistics were so often deceptive. One had but to refer to the December, 1937, issue of the *Journal of Bone and Joint Surgery* which contained three articles on fracture of the neck of the femur, and which would seem to reflect the latest expression of authoritative opinion. One of them was written by Doctor Leadbetter, presenting statistics from 1913 to 1937. The best series was one of seven cases reported by Doctor Henderson, who employed a nail, and who obtained 100 per cent union. The next best was Albee's series, who obtained 97.5 per cent union after using a tibial graft. Stein, with the abduction method, obtained 87 per cent union, and so on down to Doctor Katzenstein who had 11.5 per cent union. The British Fracture Commission, before the abduction method was instituted, reported 13.8 per cent. None of the series descended to the depressing results reported by Doctor Sauer. Doctor Whitman said his father has been very much criticized, because he himself had not reported a series of his own end-results. As a practicing orthopedic surgeon at the Hospital for the Ruptured and Crippled he saw only a very small percentage of fresh fractures. With regard to the remark that was made to the effect that Dr. Royal Whitman was responsible, in 1904, for bringing this fracture out of the limbo of complete neglect to the cynosure of surgical attention, Dr. Armitage Whitman felt that it was quite a feat, and he considered that if his father were to die tomorrow he would be satisfied with what he had done. Certainly anyone treating cases of fracture of the shaft of the femur would be criticized if he gave no idea of when the fracture was received or treatment instituted.

One discussor brought out a very good point, namely, that Doctor Thornton gets up in the middle of the night to treat these fractures as one would do if they were any other fracture. In an article by Doctor Harris, in the December, 1937, issue of the *Journal of Bone and Joint Surgery*, a series is reported, in which 76 per cent bony union was obtained by the nailing operation. Harris says that about two years ago Dr. Kellogg Speed referred to this fracture as the "unsolved" fracture. Harris says that simply by using the methods of treatment accorded any other fracture—namely, immediate accurate reposition, prolonged immobilization, and prevention of weight-bearing until such

time as the fracture has had time to consolidate which, in these cases being oblique, would be much longer than in any other—fractures of the neck of the femur would have as good opportunity of resulting in bony union as any other fractures in the body. Doctor Harris is not concerned as to whether or not the head undergoes necrosis. He has observed cases for more than three years in which this has taken place but in whom immobilization was kept up by the nail, and in which the fracture had, nevertheless gone on to complete healing.

Doctor Whitman could not believe that Doctor Wade was as pessimistic as he sounded when he remarked that "The Whitman method has shown too few satisfactory results to justify its continued use." The abduction method represents an attempt to treat a fracture, in contrast to the complete neglect in which that fracture lay at the time the abduction treatment was conceived. There can never be any question of the abandonment of the abduction method. It is proper to emphasize that the abduction method is a procedure which results in an accurate reduction of the fracture. Whether the subsequent fixation be by external means, such as a plaster of paris encasement, or by the insertion of a nail, or bone graft, is a detail which must always rest at the discretion or skill of the individual who happens to be treating a given patient.

Doctor Whitman was surprised that one of the discussers had gone back to the text-book dictum that the "first indication is to save life." He hoped that in surgical judgment surgeons had proceeded further than that. Is it not taken for granted, he asked, that any one called in to treat a patient would have as his first indication the saving of life? Abandoning statistics, Doctor Whitman concluded his discussion with the following allegory.

He had had the good fortune of serving three of his six months of medical service at The Roosevelt Hospital under Dr. Frank Jackson, a disciplinarian of the old school. A case of empyema had applied for admission to the hospital. The house physician was so sure that the patient had empyema that he turned him over to the surgeons without waiting for Doctor Jackson. Somebody suggested needling him before opening the chest. Doctor Darrach promptly said "I will," and needled him several times without obtaining pus. There were two or three cases of carcinoma of the pancreas or something equally grave waiting, and so he sent the empyema patient back to the medical service. No sooner did he arrive there than Dr. Evan Evans came in, at the head of a party of students, looking for something to demonstrate. He lit on that poor man.

Said Doctor Evans, "Why, of course he has empyema!" "The surgeons have needled him," he was informed, "and could not find any pus." "Oh, the surgeons needled him, did they? Well, give *me* a needle!" Doctor Evans tapped the patient on the back several times, with all the students standing around him, listening and watching. "It's a classical case of empyema," Doctor Evans emphasized. Confronted with a case like that, Doctor Evans was like a fox terrier after a woodchuck. All considerations of local anesthesia were abandoned. He needled this way and that way, until, at one o'clock, fortunately for the patient, the lunch bell rang. Doctor Evans and his students disappeared. Well, the poor patient looked like a strawberry cushion. Mother used to stick pins in, and was sent back to his bed more dead than alive.

At two o'clock Doctor Jackson came in again. "Any new cases, Barnum?" he asked. "Yes, a case we thought had empyema." "What do you mean, you *thought* he had empyema? Either he has or he hasn't." He whacked the patient on the chest and then put his head down. He never used a stethoscope. He used to listen to the chest through a sheet and his beard, and no one ever could find out how he could hear through his beard. "Empyema? Of course he has empyema. bring me a needle!"

"But, Doctor Jackson," protested Barnum, "this man was needled by the surgeons and then Dr Evan Evans spent two hours needling him." "Barnum, did you hear what I said? Bring me that needle!"

It was like Sidney Franklin spearing a bull blindfolded. Barnum brought the needle. Doctor Jackson thrust it in, and pulling out the plunger, obtained a syringe full of thick, creamy pus. "There you are, Barnum," he said quietly. "That will show you it makes some difference who does the needling. Next case."

DR W RUSSELL MACAUSLAND (Boston) said that up to the time when Dr Armitage Whitman spoke he had developed several good ideas but then they vanished. It must be a comfort to many to know that Dr Armitage Whitman ever served under any period of strict discipline. He could not agree with the statement that statistics mean nothing, and could not appreciate how anyone could formulate a single didactic method of treatment of this complicated fracture, varying as it does in different ages and under very differing circumstances, between the ages of 50 and 90.

It had certainly been a great pleasure to hear so many references to Dr Royal Whitman's work, for he had served under him and had held him in the highest esteem for 30 years. He so constantly preached the principles of joint care that no surgeon dealing with bones and joints today can practice without these principles, and these principles will live forever—in memory of his clear thinking and sane judgment. The statistics from the Mayo Clinic on the abduction method of treatment of fracture of the neck of the femur, as well as those of Campbell and a series of several hundred from his own clinic, are well within 1 per cent of each other as regards obtaining good bony union, which statistics were scrutinized by unbiased persons, a true evaluation, therefore, of the abduction method would appear to have been obtained. Doctor MacAusland wished that he could feel that the statistics reported relative to the nailing method were of equal valuation. Many surgeons of today, when young, were enthusiastic advocates of the open treatment of fracture. Time has mellowed that, and one must first consider the type of patient and the possible complications. He must consider the surgical technic of the operator and the institution in which this surgery is being performed, and his understanding of that particular fracture in that particular person. Certainly no law can be laid down on any classified or routine method of treatment of this fracture, other than that it first requires reduction. If one is an advocate of the open method, there are certain complications that may follow that. Many must remember the visit of Lane to this country, when metal plates were advocated in most fractures, following which for four or five years osteomyelitis had to be treated, at least all over New England. Doctor MacAusland said he had seen a lot of nailing of these fractures, indeed, some pretty good ones were just presented by Doctor Wade and by Doctor Bergamini, both of whom Doctor MacAusland wished to congratulate on their very sane presentation of the subject, but, he added, he had also seen many poor results. Why aren't they published?

One must be very careful in teaching graduates as well as students, technical methods that are to be applied to these cases and showing them one or two cases of fractured neck of the femur before and after, with a very beautiful result. They go out, and it seems so simple in the hands of expert technicians that it becomes the method of treatment in every hill town in the State. The results of that practice, even now, are not good. There has been a lot of sepsis. There have been a lot of cardiorenal difficulties, a lot of nonunion, protrusion of nails, and all sorts of complications, including deaths under anesthesia or shortly afterwards. Are these results published? A well known

anesthetist, in Boston, came to Doctor MacAusland and asked "What am I going to do? Every patient who is nailed takes 2½ hours to operate upon, many die and I cannot stand it. What shall I do?" "Carry on, if I were you," Doctor MacAusland said. "You have a good job."

MacAusland recalled the case of a Hanover Professor who was nailed and was reported as having obtained union, and represented an especially fine result. At the end of three years the man was walking with crutches, having pain, had nonunion, and he could feel the nail rattle around in his hip. There was of course a consultation and Doctor MacAusland said "It is a nonunion, the nail should be taken out and he should have some type of reconstruction performed." That upset the family and the whole apple cart. There was another consultation. No wonder. Roentgenologic examination was said to have shown trabeculae of bone growing across between the fragments. This was at the end of three years. What nonsense! Operation was imperative, and at operation when Doctor MacAusland made the incision the nail fell out on the floor, and of course there was no sign of union. Why such a report?

Doctor MacAusland said that, although heartily in sympathy with the method, he was not yet convinced that it was the only method, or that the best technic had been developed. He expected to use it more than he has been doing, but was going about it very cautiously. He expressed himself as very definitely against the wholesale teaching of this method, however, as a "cure" for fractured hips because it isn't so, and the statistics that have been reported thus far are not any better, and some not as good, as those obtained by conservative treatment, and many are not true reports!

Some few years ago Doctor MacAusland happened to go on a cruise in which there was a symposium on the treatment of tuberculous joints. The speakers were very carefully selected. They all had the same mind as to what should be done. The only question was who could get them first and fuse them. He listened to this symposium for one and one-half or two hours, and said that he was very glad to have heard the papers, but felt perfectly sure that Doctor Bradford, his old Professor at Harvard, and an advocate of conservative treatment, must be turning over, face downward, in his grave if he could hear. It didn't seem possible that such treatment could be advocated in such a wholesale manner in every case, and Doctor MacAusland feared that he must say the same thing about fractured neck of the femur. He was definitely opposed to any open operation on patients 80, 85, 90 or 95 years old, that takes so much time and has many pitfalls. He still believed the abduction methods have a very definite place. Certain forms of new traction methods have promise, while he would not care to report his results with this new method as yet, it is certainly as satisfactory as any other procedure and it is distinctly more simple.

DR PRESTON A WADE (New York, closing) remarked that with one fact, apparently, everyone was in agreement, namely, that subcapital fractures, impacted in the valgus position unite regardless of what form of treatment is employed. Answering Doctor Gordon's question as to what method he would advocate, since he felt the Whitman method was unsatisfactory, Doctor Wade said he was not advocating any operative method at the present time, because he had not had a large enough series of cases to prove that operative methods were more satisfactory than the older procedures. At the present time many surgeons are trying out various operative methods, as indicated in recent literature—reconstruction operations, pins, Smith-Petersen nails, *etc*. Even Leadbetter states that he is now performing internal fixation in 75 per cent of his cases.

In reporting this series of very poor results following employment of the

Whitman method, Doctor Wade said he meant no disrespect to Doctor Whitman. These cases were treated by 31 different surgeons, and it is helpful to report their results. Doctor Sauer's report of results of treatment in these cases at City Hospital included the cases which received primary treatment from many of the other hospitals in the City. Many of these cases were transferred to the City Hospital during the period of immobilization. They remained at City Hospital for long periods of time, so that end-results were seen.

DR HERBERT M. BERGAMINI (concluding) quoted the following poem

THE SMITH-PETERSEN PIN*

A great aunt of mine,
Of age sixty-nine,
Admittedly rather a dreamer,
One day in her flat,
Fell over the cat,
And fractured the neck of her femur

Doctor Whitman was called,
Who at once was appalled
And made ready to put on a cast
Although a relation,
A new consultation
I requested without being asked

It was held the next day,
And on the x-ray
The bone was in fair apposition
So they seized the old dame,
Strapped her on a hard frame,
As they did in the French inquisition

Soon that great aunt of mine,
Like an old porcupine,
All tied up with bandage and rope,
Lay bustling with pins
While I for my sins
Supplied the appropriate dope

In short she got well,
And I shudder to tell
Any facts that are not strictly true,
She's amazingly supple,
And one of a couple
Of tap dancers in a revue

If you're one of the number
Who, dancing the rhumba
Or after a surfeit of gin,
Fall like my relation,
Without hesitation
Demand a Smith-Petersen pin

* Author unknown. Original source from a patient who found it somewhere.

BRIEF COMMUNICATIONS AND CASE REPORTS

PARATHYROID TUMOR

REPORT OF TWO CASES

ARTHUR S McQUILLAN, M D

NEW YORK, N Y

Case 1—M C, female, age 46, married, born in Poland, was admitted to Bellevue Hospital October 28, 1932, and was discharged November 10, 1932, with a diagnosis of nodular goiter (adenoma of the thyroid)

Chief Complaint—Swelling on the outer aspect of neck *Family History*—Negative as far as goiter was concerned *Present History*—This dated back 12 years, when patient noted difficulty in swallowing following childbirth Five years later she noticed a swelling in the right side of her neck which gradually increased in size It regularly became enlarged during menstrual periods There was no tachycardia, no difficulty in swallowing, no nervousness or tremor Patient had taken iodine off and on for the past year B M R was within normal limits Menstrual history was negative Patient had nine children, seven of whom are living

Physical Examination—Well nourished woman of 46, good color, weight, 140 pounds, pulse averaged 80, blood pressure, 140/80, lungs, negative, heart, normal in rate and rhythm corresponding with pulse, sounds of good quality, soft systolic murmur at the base In the region of the right lobe of the thyroid there was a swelling about the size of an orange, somewhat nodular, which moved with swallowing There was a high pitched bruit heard on the upper surface of the neck There were no tremors Urine negative Wassermann negative

Operation—November 1, 1932 Under gas-oxygen-ether anesthesia, what was thought to be the right lobe of the thyroid was found involved by a degenerated nodular mass, which was covered by many large veins It was, however, removed without difficulty The left lobe of the thyroid was found to be normal The postoperative diagnosis was nodular goiter The wound healed by primary union and the patient was discharged from the hospital on the ninth day postoperative

Pathologic Examination—Doctors Slaughter, Rottino and Symmers The gross specimen consisted of a mass of tissue 9x6 cm (Fig 1) There was a thin transparent capsule, the underlying tissue having a pink color There were many prominent veins On section the surface was smooth and homogeneous Microscopically, the mass was found to be composed almost entirely of oxyphil cells (Fig 2) *Pathologic Diagnosis*—Parathyroid adenoma

The patient was later readmitted to the hospital where roentgenograms of the bones of the skeleton were found to be normal Blood calcium determination of 10.2 and blood phosphorus determination of 4.2 were within normal limits Phosphatase was not determined

Since operation, this patient has remained in excellent health There has been no recurrence of the tumor A recent examination showed normal values for calcium, phosphorus and phosphatase

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The majority of parathyroid tumors reported in the literature have been associated with bone and blood changes. Also, most of the tumors reported are of the clear cell type rather than the oxyphil type as shown in this case.

The case is presented to illustrate a parathyroid adenoma made up almost wholly of oxyphil cells, in whom both the bones and blood chemistry were normal.

Case 2—A S C, female, age 53, single, was first examined in July, 1935, at which time a swelling was noted involving the right thyroid region. This had first been noted by the patient two years previously and had been increasing slowly. There was a history of nervousness and fatigue over a period of several years. There had been no loss in weight or any complaint of cardiac disturbance.

FIG 1

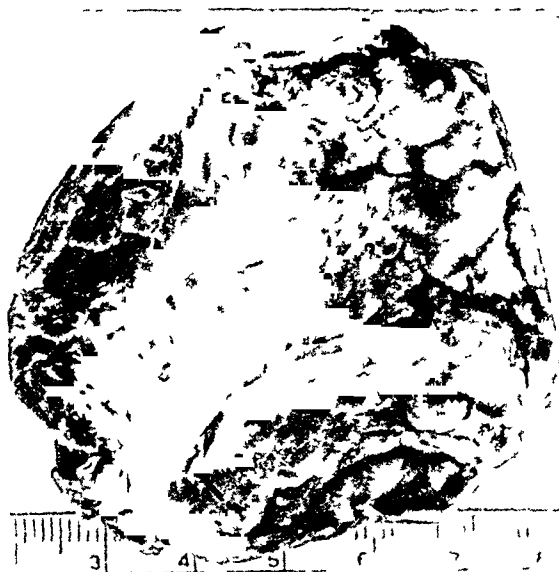


FIG 2

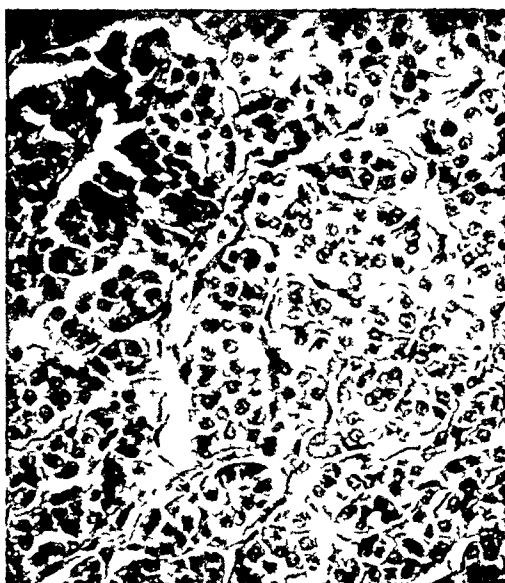


FIG 1—Case 1. Photograph of the gross specimen. Note the capsule in left marginal area.
FIG 2—Case 1. Photomicrograph of a section of the parathyroid tumor showing the cells well outlined, and the cytoplasm granular and oxyphilic. Note the absence of clear or chief cells.

Physical Examination showed a two-inch nodule with a small area of what was thought to be calcification along the inner border, involving what appeared to be the right lobe of the thyroid gland. The weight at this time was 109 pounds (no loss), pulse, 80, and regular, blood pressure, 110/80, B M R, -14, which might be considered a low normal. *Diagnosis*—Nodular thyroid (or adenoma).

A diagnosis of nodular thyroid (or adenoma) was made, and operation for excision of this tumor was undertaken August 24, 1935.

Operation—August 24, 1935. An encapsulated tumor the size of a golf ball, and firmly adherent to the trachea, was found, which apparently involved the right lobe of the thyroid gland. In order to facilitate the removal of the tumor, it was necessary to excise the entire thyroid lobe. On section, the well developed capsule was strongly adherent to the tumor tissue, which was of the consistency of liver and had a yellowish-gray appearance. It was quite evident that the tumor was not a simple thyroid nodule (or adenoma).

Pathologic Examination—Dr. H. R. Muller. *Gross*—"A spherical mass, about the size of a golf ball. It is covered with a thin fibrous capsule. The consistency is rubbery, but not very hard. The cut surfaces are homogeneously pinkish-gray. In one portion is some calcified material." *Microscopic*—The tumor is composed chiefly of very

FIG. 4



FIG. 3B

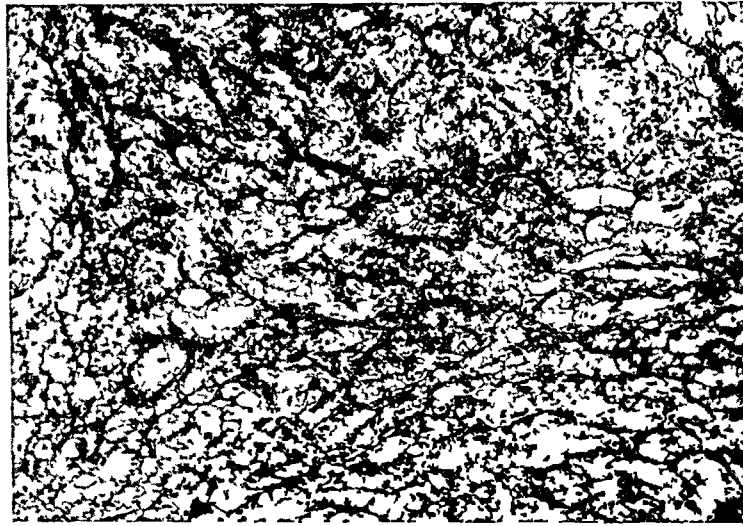


FIG. 3A



FIG. 3—Case 2 (A) Showing the lawless arrangement of cells. Note the predominance of clear cells with small nuclei. The darker stained cells are oxyphilic. (B) Note the predominance of clear cells.
FIG. 4—Case 2. Section of the metastatic nodule attached to the external jugular vein. Note the presence of both clear and oxyphilic cells, also invasion of the capsule.

large cells, with clear, slightly foamy cytoplasm and with a single small round compact nucleus. The outlines of the cells are distinct. Many cells show an area of pinkish material occupying a portion of the cell. A delicate connective tissue reticulum, bearing capillaries, runs around small groups of these cells or acts as a supporting structure. In some portions the cells are small and very acidophilic, but with the same histologic structure. There are also areas of necrosis. The capsule around the tumor varies in thickness, being very thin in places. Outside of the capsule, in one section, is some thyroid tissue consisting of moderately dilated acini filled with colloid and having a low cuboidal epithelium. The structure of this tumor is unusual and suggests an adenoma of the parathyroid (Fig 3A and B). *Pathologic Diagnosis*—Adenoma of parathyroid."

Calcium and phosphorus determinations, as well as skeletal roentgenograms, were then made and found to be normal.

Subsequent Course—The patient made a good recovery, gained weight, made no complaints, except for occasional painful joints, until August 27, 1937, two years following operation, at which time there appeared a slight fulness in the right side of the neck, and the presence of a small, hard nodule, apparently involving the skin and subcutaneous tissue adjacent to the right external jugular vein on a level with the thyroid cartilage. Physical findings were otherwise negative. There was no loss of weight.

On September 10, 1937, this small nodule was excised under novocain. It was found attached to the external jugular vein. The tissue was friable and gray in appearance.

Pathologic Examination—Dr. E. S. L'Esperance, Gross—"Specimen is an irregular, ragged mass of yellow and grey soft tissue, two centimeters in greatest diameter. *Microscopically*, the sections show a partially encapsulated tumor composed of cells resembling those of the adrenal cortex. The cells, for the most part, are large with round or oval vesicular nuclei. A few have opaque eosinophilic cytoplasm. There is a tendency to glandular arrangement (Fig 4). *Pathologic Diagnosis*—This is probably an adenoma of the large cells of the parathyroid. It does not appear to be highly malignant."

Subsequent Course—On December 11, 1937, after roentgenotherapy (four treatments) there was not only a recurrence of the nodule at the site of excision, but there was found another small nodule on a slightly higher level and nearer the median line of the neck, apparently lying superficially in skin and subcutaneous tissue.

On December 31, 1937, roentgenologic examination of the complete skeleton was found to be normal, as was a recent determination of calcium (107), phosphorus (33), and phosphatase (27).

This case is presented as an instance of a malignant tumor of the parathyroid gland, the malignancy based on metastasis rather than on individual cell characteristics. There were no abnormal bone or blood chemistry findings in association with this tumor, which is contrary to some of the reported cases.

DISCUSSION—DR. EMIL GOETSCH (Brooklyn) felt that Doctor McQuillan's cases represented another confusing syndrome. Here parathyroid tumors were found but there were no associated changes in the bones such as one might be led to expect. The great size of the parathyroid tumors was certainly unusual, the first being about the size of an orange, the second of a golf ball. Doctor Goetsch cited a personal experience he had many years ago with a parathyroid tumor, at least it was so considered after careful studies as large as a grapefruit, which caused paroxysms of coughing due to tracheal compression. Calcium studies were not made at that time.

In Doctor McQuillan's first case, the histologic section resembled very much the appearance of a thyroid adenoma. In the second case the tissue

was clearly that of a parathyroid gland. The failure to find incidental bone changes is usually important, and may point to a differentiation in the function of the two main types of cells occurring in the parathyroid gland.

DR HENRY L. JAFFE (New York) said that a number of tumors, similar to those found in Doctor McQuillan's first case, had been described during the last few years—namely, enormous oxyphil cell adenomata of the parathyroid. The fact that the cytoplasm of the adenoma cells is oxyphilic is offered as the explanation of why these tumors do not demineralize the skeleton, that is, they apparently do not secrete parathormone. It would be of great importance to assay such tumors for the presence of parathormone. One really does not know whether these tumors are parathyroid tumors or not.

DR ARTHUR S. MCQUILLAN (New York) closing said, in connection with his first case, which Doctor Jaffe discussed, that Keynia, in the British Journal of Surgery, October, 1936, described a case essentially similar, which was made up almost entirely of oxyphil cells, and which evidenced no signs or symptoms of hyperparathyroidism. Keynia cited four other somewhat similar cases and suggested, as did Doctor Jaffe, that possibly these cells are inactive, with low function of secretion and, therefore, one should not expect bone changes.

With regard to malignant tumors of the parathyroid gland, Doctor McQuillan said he had searched the literature and could find only 19 cases of proven malignancy of the parathyroid gland and not all of these were proved by metastases. Diagnosis in some was made on the cell morphology, which is considered difficult, as is the tissue diagnosis of carcinoma of the thyroid gland. All of the 19 cases, except two, did not show any changes in the bones or blood chemistry. The Mayos reported a case, in 1929, of malignancy of the parathyroid gland associated with bone and blood changes. They later reported a case, in 1934, showing the same changes, and in both cases the diagnosis of malignancy was made on cell morphology and not on the presence of metastasis.

THE TREATMENT OF ACTINOMYCOSIS WITH THYMOL *

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NEW YORK, N. Y.

IN REVIEWING the literature relative to the incidence and methods of treatment of actinomycosis, the following was found. An analysis of 500 cases showed the distribution of the lesions to be: head and neck, 55 per cent, thorax, 20 per cent, abdomen, 20 per cent, and it had occurred in the lower jaw incident to caries of the teeth. Actinomycosis produced the following types of lesions in the region of the appendix: (1) Painful tumor, (2) gangrenous appendix, (3) perforation of the cecum.

Actinomycosis is thought to be contracted from chewing straw, wheat or rye. Various treatments have been tried. Potassium iodide in doses up to 120 gr. or more, wet dressings of copper sulphate $\frac{1}{2}$ to 2 per cent solution, deep

* Presented before The New York Surgical Society, February 23, 1938. Submitted for publication April 11, 1938.

roentgenotherapy has been of advantage in some instances. Gautier, in France, has developed an electrotechnical method of therapy. He inserts two platinum needles into the infected areas which act as poles between a constant current of 50 milliamperes, and at the same time 10 per cent potassium iodide is injected continuously by the drop method into the mass. The current decomposes this solution into nascent iodine and potassium.

In the present instance, roentgenotherapy was finally decided upon. This had not been considered before because of the possibility of adding sterilization to the other troubles of the patient. Just before the treatment was to be instituted, Dr. H. B. Myers,¹ of Portland, Oregon, published an article describing the use of thymol as a specific for actinomycosis in which he advised adequate surgical drainage of the local lesions and a packing of 10 to 25 per cent thymol in olive oil and tolerance doses of the crystals by mouth to prevent the spread of the disease to other parts of the body.

Case Report—Hospital Chart No. 61057. A. F., white, female, age 20, was admitted to the City Hospital, New York, complaining of discomfort in the right lower abdominal quadrant and the presence of a persistent sinus which opened into the scar of the previous appendicectomy wound.

Previous History—In 1933, the patient, age 15, had been operated upon at the Wyckoff Heights Hospital, Brooklyn, N. Y., for acute appendicitis, but the wound never healed.

Postoperative Diagnosis—Gangrenous appendicitis with local peritonitis. It has not been possible to obtain a pathologic report of the appendix.

Subsequent Course—In December 28, 1936, she was again operated upon at the City Hospital, N. Y., by Dr. Ward Renfrew, and the sinus tract dissected out and an ovarian cyst removed. The wound healed, but one year later, December 28, 1937, she was readmitted with a preoperative diagnosis of acute osteomyelitis of the crest of the ilium. This area was incised and drained. Pathologic examination of tissue removed showed actinomycosis. The wound continued to drain and the patient was given large doses of potassium iodide—up to 120 gr. a day. On March 30, 1937, an abscess in the abdominal wall, in the region of the McBurney incision, was opened, but never healed.

She was first seen by our service on April 1, 1937.

Physical Examination—The patient was thin and emaciated, lying in bed with her right knee drawn up and the right thigh flexed on the abdomen. Weight 70 pounds. She was very apprehensive and frightened. A draining sinus was present at the lower end of her appendix scar, with marked tenderness and induration around it. Over the crest of the ilium there was a broad wound covered with sluggish granulations.

Operation—April 16, 1937. Following a transfusion, the sinus tract leading downward from the lower end of the scar of the McBurney incision was explored. Boggy, granulation tissue was found throughout and the femoral vessels were embedded in it. The tissues bled very freely and the hemorrhage was hard to control. She was subsequently transfused twice because of a severe hemorrhage which occurred at the time of the primary dressing. No improvement followed.

Second Operation—May 13, 1937. This same area was dissected out, only more extensively. It was found necessary to ligate and sever the femoral artery and vein above Poupart's ligament in order to eradicate the involved tissue. The wound extended down to the space of Retzius. An area in the thigh, below Poupart's ligament, was also opened and drained. Notwithstanding the ligation of the femoral vessels, there was never any sign of disturbance in the circulation of the leg. She nearly died during the above operative procedure and had to be transfused immediately postoperatively.

Postoperative Course—The patient became progressively worse. She could not

eat, cried almost constantly from pain, and showed a complete loss of morale. During the last week in May, 1937, her condition had become so serious that roentgenotherapy was considered. However, just at this time the article by Myers¹ appeared, suggesting the employment of thymol. This treatment was immediately instituted, June 2, 1937, and the sinuses were packed with 20 per cent thymol in olive oil. She received 10 gr of the crystals every other day. Larger or more frequent doses produced a gastroenteritis. On June 20, 1937, and again on September 8, 1937, areas of infection in the outer side of the thigh were opened and packed. At the first operation it was found that the sinus tract at the lower end of the McBurney scar also opened into the posterior vaginal fornix.

Results of Thymol Therapy—The change in the appearance of the sinus tracts, after packing with thymol, was remarkable. In a very short time they had lost their "drippy," dirty appearance and the granulations became pink, dry and clean. From week to week healing could be seen, especially in the sinus tracts treated with thymol after they had been freshly opened and drained. The temperature dropped immediately. After the operation on June 20, 1937, her progress was very steady. She got up in a wheel chair and then walked with crutches. As soon as she was able, she was sent daily to Occupational-Therapy and allowed out all day in the sun. By September, 1937, the contraction in her knee had disappeared and she walked normally with full range of motion. She has had Alpine light treatments three times a week and transfusions when necessary to keep her hemoglobin within normal range. At present, her sinus tracts are closed except for three. A small one on the anterior surface of the thigh, one on the outer side of the thigh, and the pelvic one which has healed a great deal during the past month. She has a tender, swollen area on the inner side of her thigh which will have to be opened soon, probably an extension of the disease through the obturator foramen along the adductor group of muscles.

The general condition of the patient is good. Her weight is now 107 pounds, a gain of 37 pounds. This new abscess is localized, and certainly the outlook for its eradication by the use of thymol is very much better than it would have been a year ago when her condition was so poor and there seemed to be no prospect of staying the progress of the disease. The red blood count averages about 3,500,000, the hemoglobin between 55 and 75 per cent. The white blood count has averaged about 15,000 with 74 per cent polymorphonuclears. The urine, which during the acute part of her illness showed albumen and casts, has now cleared almost entirely and shows only a faint trace of albumen. This fall, her menstrual periods, which had stopped for seven months, began again and are quite normal.

SUMMARY

(1) In the case herewith reported, great benefit was derived from the use of thymol by mouth and thymol in oil packed into the wounds after adequate surgical drainage has been established.

(2) No benefit has been derived by the excessive doses of potassium iodide.

(3) The immediate drop in temperature after the administration of thymol, and the later gain in weight, have been evidences of the therapeutic value of thymol.

(4) It is obvious that the patient is not cured, but her condition is certainly vastly better than it was before the administration of this agent.

REFERENCE

- ¹ Myers, Harold B. Thymol Therapy in Actinomycosis. JAMA, 108, 1875, May 29, 1937.

DISCUSSION —DR THOMAS H. RUSSELL (New York) cited the following case. A white, Jewish male, age 28, was operated upon in Florida for a ruptured appendix. He felt well for a few weeks, but then his temperature rose and a diagnosis of subphrenic abscess was made and the abscess drained. He improved, but four months later because of a temperature of 102° F the subphrenic abscess was reopened and drained. Following this his temperature did not come down to normal, and he was admitted to New York Post-Graduate Hospital for reexploration of the subphrenic abscess. At operation, January 20, 1937 the subphrenic area was explored. No pus was found but a moderate amount of necrotic material was removed from the sinus and subphrenic area. Since then there has been a small amount of discharge from the tract. Scrapings from the sinus tract revealed purulent exudate with associated colonies of actinomycosis. Gastro-intestinal roentgenologic studies, February 10, 1938 revealed a rather narrow, constricted terminal ileum, somewhat segmented suggesting chronic hypertrophic changes in this segment. Roentgenograms of the lung showed subphrenic pathology, moderate lung retraction on the right side with fluid at the right base, and a partial hydro-pneumothorax. For the past six days the patient has been treated with thymol taking 2 Gm daily by mouth and the sinus being irrigated with 15 per cent thymol solution in olive oil.

DR ALLEN O. WHIPPLE (New York) said that he had had one patient who was proving a very interesting problem who had a very diffuse distribution of actinomycotic lesions. The difficulty was that he had had a number of therapies instituted, as is so often the case in these desperate lesions, and it was very difficult to determine just which therapy had had the most pronounced effect. Thymol regimen would have been pushed much more vigorously had the patient tolerated it better. Tolerance should be determined, as some patients are quite intolerant to the large doses employed. There are several ways of administering thymol. Taking it by mouth upsets some patients so that they cannot take food. The case just referred to was up and about with a new focus, and he thought the excellent result largely due to the indefatigable and constant attention of the house surgeon who had really done a remarkable piece of work in keeping after the patient. Undoubtedly thymol has a very real place in the therapy directed against this condition.

DR M. STANLEY-BROWN (closing) said that in Dr. H. B. Meyers' description of the use of thymol there was one case included, in the six reported, which did not turn out favorably because the patient could not tolerate the thymol by mouth. The local lesion cleared up but the patient developed actinomycosis of the lung from which he eventually died. Where the thymol is tolerated it seems to work very well. Doctor Meyers stressed the point that the affected areas must be opened, afforded adequate surgical drainage, and packed with thymol in olive oil to give the best results. The patient presented weighed 70 pounds when first seen, and had been in the hospital for several months with no change. After thymol was instituted she gained weight and her temperature dropped, it would seem to be the effect of the thymol therapy that brought about the improvement. She tolerated 10 Gm every other day but if this amount was increased some difficulty was experienced.

REVERSED COLLES' FRACTURE

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PHILADELPHIA, PA

THERE is a discussion in the literature, Webb and Sheinfeld,¹ Raymer,² Bettman and Tannenbaum,³ Wood,⁴ Greeley and Hobart,⁵ on the question of whether or not reversed Colles' fracture can be reduced and held, without resort to open operation. It has been of interest to study the photographs published by these authors, in conjunction with the five cases, shown in Figures 1, 2, 3, 4 and 5, from the Episcopal Hospital records

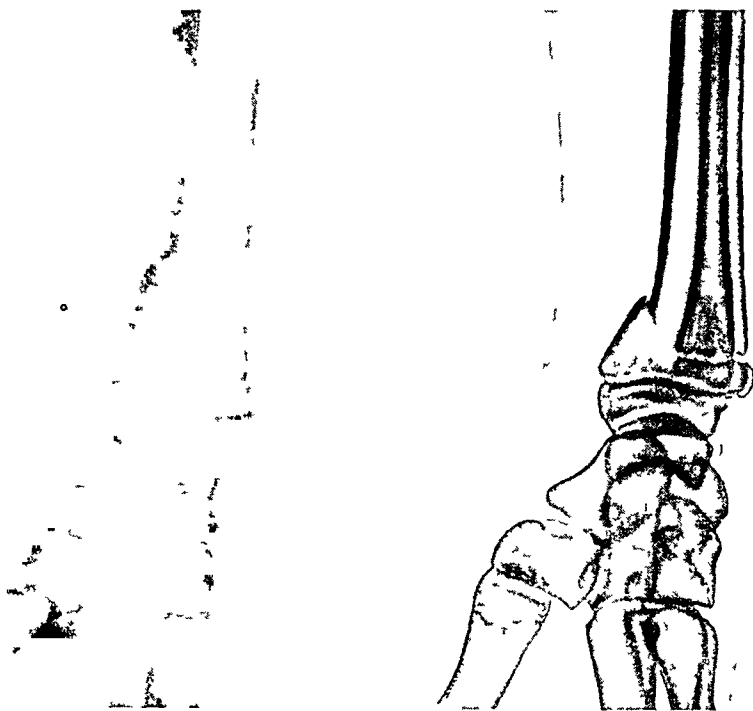


FIG 1—B R age 11 Greenstick fracture in distal end of diaphysis with slight palmar displacement of fragment A true reversed type

It is important for the proper understanding of this lesion to realize that we are dealing with two rather distinct conditions. Some of them are true reversed Colles' fractures, others are anterior fracture-dislocations of the wrist. The true reversed Colles' fracture is very well shown in Greeley's and Hobart's⁵ Figure 7B, in which dislocation is absent, and in which the fragment is displaced at an angle to the shaft. The fracture-dislocation type is equally well shown in their Figure 1, in which the wedge-shaped fragment from the lower lip of the articulating surface of the radius is approximately parallel to the anterior surface of the shaft. It has been forced proximally away from the line of the radiocarpal joint. Comminution of the fragment may produce an intermediate type, as shown in Figure 4.

REVERSED COLLES' FRACTURE

This fracture-dislocation bears some resemblance to fracture of the dorsal lip of the radius. Both of these lesions represent fractures of overhanging bony lips. The difference in the two is to be found in the fact that the dorsal lip of the radius overhangs the radiocarpal joint, while the anterior lip is approximately flush with the articulating surface, but overhangs the anterior surface of the shaft of the radius. These two lips protrude approximately at right angles to each other.



FIG. 2.—D. O., age 13. Epiphyseal separation anteriorly. A true reversed type.

In fracture of the anterior lip, the integrity of the joint is destroyed, and the carpus is easily displaced along the anterior surface of the shaft. In fracture of the dorsal lip, it is rare for dislocation to occur, because of the intimate relationship which the strong flexor tendons bear to the anterior surface of the carpus. These tendons turn sharply about the lower end of the radius in dorsal flexion, and unless the entire lower end of the radius is fractured and displaced, the carpus cannot be forced dorsally while in dorsal flexion. A dislocation of the carpus in dorsal lip (Barton's) fracture would,

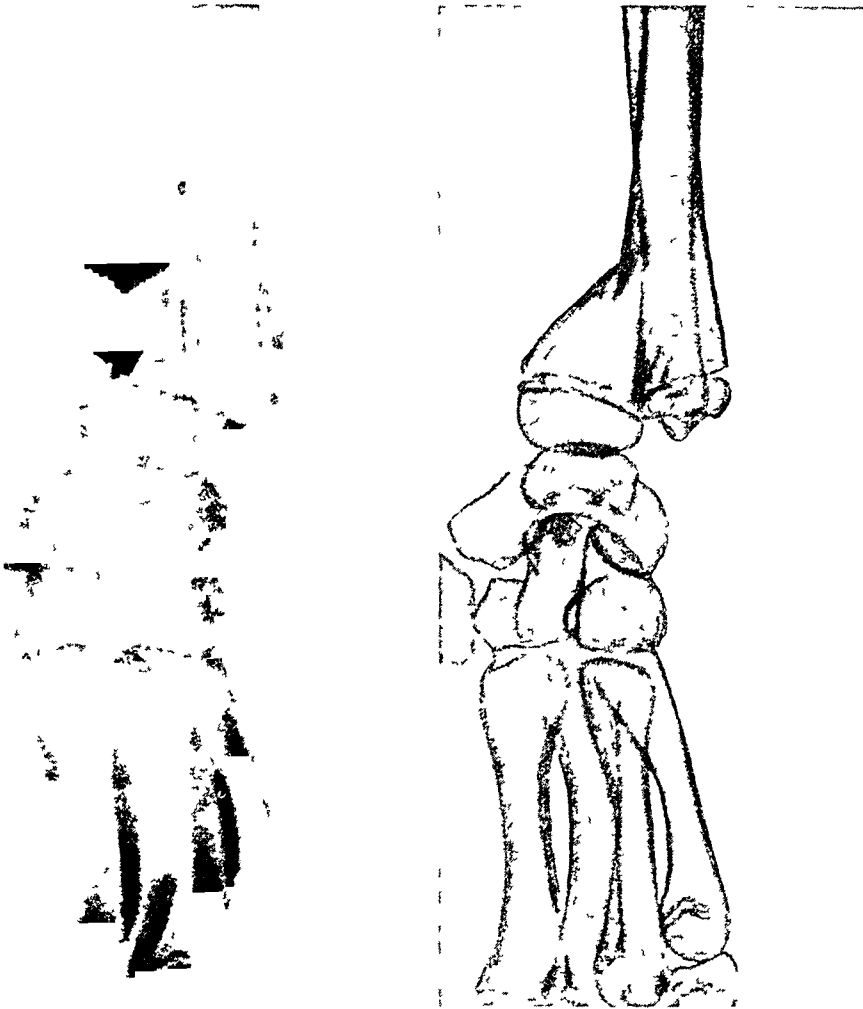


FIG 3—E W, age 13 Epiphyseal separation anteriorly A true reversed type



FIG 4—I B, age 67 An intermediate type The anterior lip of the radius is broken off but the fracture line also passes completely through to the dorsum This intermediate type is formed by the comminution present

of necessity, be at a right angle to the tendons. In the anterior fracture-dislocation, the dislocation is in line with the tendons and the fragment can slide along them.

The closed reduction and fixation of fracture-dislocation is conceivably more difficult than it is in the case of the true reversed Colles' fracture.



FIG. 5.—M. G., age 45. Anterior fracture dislocation of the wrist. The fragment is parallel to the shaft of the radius. The anterior lip of the radius is fractured and driven proximally.

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MEMOIR

EDWARD MARTIN

1859-1938

DOCTOR EDWARD MARTIN, the youngest son of Jonathan Willis and Malvina Regester Martin, was born in Philadelphia August 14, 1859, and died in the same city, March 17, 1938 His preliminary education was ob-



EDWARD MARTIN M D

tained in the public schools of this city and for a short period at Central High School. He attended Swarthmore College four years, ranking first or second in all classes and was elected to Phi Beta Kappa. He was graduated in 1878, *Magna cum laude*, obtaining the degree of A B. at that time and later (1882) A M. and (1920) D Sc. from this college. He was graduated from the medical school of the University of Pennsylvania in 1883, from which institution he later received the degree of LL D., and served as assistant to Dr. D. Hayes Agnew and later to Dr. J. William White. For a few years he practiced medicine and then devoted his time to working in the fields in which he ultimately specialized—genito-urinary and general surgery. He was a prolific writer, being the author of several authoritative text-books on surgical subjects, sections for medical systems, editor of the University Medical Magazine and Surgical Editor of The Therapeutic Gazette, as well as the author of innumerable papers read before various medical societies and associations. He was a true teacher, with the ability to so present his thoughts that he indelibly impressed them upon his listeners.

His loyalty and affection to Swarthmore College and the University of Pennsylvania were outstanding—nothing that he could do ever seemed to be enough, in his estimation, to repay these two institutions for what they had done for him. He worked indefatigably for them in every way that he could. His motto was "The Best Is Yet to Come", and with this in view he worked and planned to the last for work in the Edward Martin Biological Laboratory at Swarthmore, which laboratory was really a tribute to the lasting friendship existing between Mr. Fred M. Kirby and Doctor Martin, and was made possible by Mr. Kirby's generous million dollar gift for this purpose.

Another permanent memorial to this friendship was the Kirby Fund, founded by Mr. Kirby for the benefit of students who needed financial aid to complete their medical course. It was instituted after Mr. Kirby heard Doctor Martin tell of a student who tried to work his way through medical college and died in the effort. Under this Fund students were enabled to borrow such money as they required, paying it back to the Fund as soon as they became able to do so. He helped financially, and through his influence obtained scholarships for more than one young man—and these men have since achieved success in the medical and other professions, thanks to his efforts and encouragements.

He was a pioneer in many lines—prior to the Wright brothers' achievements, he and Dr. Paul Chamberlin conducted a number of experiments to prove air flight possible. He also was interested in the Eastman Kodak Company from a teaching standpoint and made several trips to their plant in Rochester, N. Y., to supervise the taking of educational films—one of which dealt with appendicitis—to be used in the medical schools. He was a pioneer in the use of the lantern slide and later movie films for student teaching.

He was the first man in the University of Pennsylvania Hospital to use

morphia after an abdominal operation, and to Doctor Martin we owe the deep breathing exercises to prevent postoperative pulmonary complications, which practice has withstood the test of time and is today used even more commonly than CO₂ inhalations. He early practiced the "no-touch" or instrument technic in surgery, using white cotton gloves as telltales on the offender. Gentleness in the handling of tissue was his continual admonition.

In all things, Doctor Martin believed in preparedness, and this, with his ideas on loyalty, honesty of purpose, kindness, tactfulness and consideration in the handling of his patients, constituted his creed. He was honest with himself and others in all his dealings, a strict disciplinarian, yet most charitable to the failings of others.

Doctor Martin had many allied activities in public enterprises. It was through his efforts that typhoid fever was stamped out during the Spanish-American War, he was Director of Health and Charities in Philadelphia under Mayor Weaver, from 1903 to 1905, Commissioner of Health in Pennsylvania, from 1918 to 1923, under Governor William Sproul (a classmate of his at Swarthmore), he inaugurated the Traveling Dental and Prenatal Clinics, did special work regarding syphilis and gonorrhea, instituted the use of toxin-antitoxin for preschool age children, and of antitoxin early in diphtheria, was responsible for schools of instruction held one week each summer for State Inspectors. The Philadelphia Health Council and their good work against tuberculosis are the result of his efforts.

Since 1885, he was a member of the Board of Managers of Swarthmore College, a member of the Board of Education, since 1911, and its President at the time of his death. He was elected Clinical Professor of Surgery at the Women's Medical College of Pennsylvania, in 1902, resigning after several years. He was Professor of Clinical Surgery at the University of Pennsylvania, 1903 to 1910, and John Rhea Barton, Professor of Surgery at the same institution, from 1910 to 1918. He also served the University of Pennsylvania as Professor of Surgical Physiology. He was Chief Surgeon to the University of Pennsylvania and the Howard Hospitals, from 1910 to 1918, and consulting surgeon to Bryn Mawr Hospital, Norristown State Hospital for the Insane, State Hospital for the Insane at Wernersville and the Philadelphia General Hospital.

He was a Fellow and Regent of the American College of Surgeons and former president of the Clinical Congress of Surgeons, a member of the American Philosophical Society, American Surgical Association, Clinical Society of Surgeons, American Association of Genito-Urinary Surgeons, and of several foreign surgical societies, as well as the local state and county organizations. Incidentally, he was a member of the Philadelphia County Medical Society for 54 years and received a framed certificate to that effect which he prized very highly. In 1935, Temple University conferred on him the degree of D Sc.

Doctor Martin's war record covered a period of many years, he having been a Reserve Officer for some years and in the O R C several years be-

fore the World War His active service in the World War began in Philadelphia January 1, 1918, although he had been a member of the Medical Section, Council of Defense, from the beginning of the war He was lieutenant, major, lieutenant colonel, colonel, reserve officer of the World War—364th Medical Regiment, O R C , U S A , Regimental and Brigade Surgeon, Spanish-American War, Surgeon and Major in Third Regiment National Guard of Pennsylvania for 12 years in the early nineties, Director of School of Surgery, Fort Oglethorpe, Ga , also Chief of Surgical Section of Hospital He was the first director of Base Hospital No 20 of the University of Pennsylvania, however, he was soon called back to Washington, being succeeded by his assistant, Dr J B Carnett, who carried it to its fruition Doctor Martin was Chairman of States Committee, School of Surgery, University of Pennsylvania, for Medical Officers of the Army, Director of Professional Service and Surgical Chief, Walter Reed Hospital, Chairman of States Committee, Advisory Board Medical Section Council of National Defense He was honorably discharged from the service January 27, 1919

Athletics always aroused his greatest enthusiasm He was on a winning crew of the University of Pennsylvania in the eighties played tennis fished, and in later years was an ardent golfer At the close of the football season he acted as host to the entire football squad of Swarthmore College, giving a traditional dinner at The Lamb's Tavern with the main feature on the menu being a suckling pig with a red apple in its mouth!

For a number of years, beginning in 1903, Doctor and Mrs Martin entertained children from the city slums at Valley Farm, a short distance from their Orchard Farm These youngsters were exceptionally well cared for during their stay and were returned to their homes after a vacation of a week or two, Girl Scouts have occupied a part of Doctor Martin's farm for several years, his cousin presiding as hostess For the past 20 years, Doctor Martin spent his winters in Florida, his summers at Orchard Farm, Media, Pa, and about a month at his home in Graefenburg Springs in the beautiful South Mountain part of the Blue Ridge chain There were many deer here and he planned to give this estate to the State as a game preserve after the death of Mrs Martin and himself

He was a member of the Juy, Rittenhouse, Pine Valley Golf, Rolling Green Golf and Seaview Golf Clubs

Endowed with a keen, quick sense of humor, Doctor Martin, with his six foot one inch straight soldierly carriage and dark auburn hair, was much in demand among his friends and professional colleagues, excelling alike as speaker, toastmaster or host—he was never at a loss for the appropriate word or expression in any situation He was extraordinarily clever as a correspondent and always kindly, sympathetic and helpful to those who were fortunate enough to come in contact with him He was quick to sense any possible talent in those in whom he was interested and would do all in his power to bring such talent to perfection The death of his wife last fall after many years of companionship was a great loss to him

And so lived a great man—a true servant of the public—whose virtues often escaped the superficial observer as is true of so many of the world's kindest and most helpful members whose sincerity and naturalness lead them to hide their real selves behind a "smoke screen" to escape embarrassing acclaim. Of no one was this more true than of that Hicksite Quaker—Edward Martin.

ELDRIDGE L. ELIASON

EDITORIAL ADDRESS

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MEETING HELD AT ATLANTIC CITY, N J

MAY 2, 3, 4, 1938

ADDRESS OF THE PRESIDENT THE RELATION OF SURGEON AND HOSPITAL

ARTHUR W ELTING, M D

ALBANY N Y

FOR THE great honor and distinction which you conferred upon me last June in selecting me to be your presiding officer upon this occasion, may I again express my sincere gratitude and appreciation?

The preparation of the address which your president is expected to deliver has been my chief anxiety and concern during the past year. In the hope of finding some inspiration from the thoughts of my 55 illustrious predecessors, I have carefully perused their addresses.

I find that in the main they may be divided into two groups. Those in which purely surgical topics have been discussed, and those in which some of the more general problems confronting the surgical profession have been considered. It seemed to me that at the present time it might be more profitable to discuss some of the problems that belong in the latter group.

Much attention has from time to time been given to *what* should be the education and training of a surgeon, notably in the addresses of some of our more recent presidents. To this at present little, if anything, can be added. In all this thought and discussion as to *what* should be the education and training of a surgeon, very little, if any, attention has been given to *where* this can or should be accomplished. Perhaps it has been assumed that we already possess enough hospitals of high standards in which these young men could be trained, or if not that they would soon come into existence. A care-

ful survey of the hospital facilities of this country at this time demonstrates conclusively that both these assumptions are fallacious

There are at the present time in this country comparatively few hospitals where adequate training can be had and it will require much time, thought, organization and hard work to bring the standards and administration of a sufficient number of hospitals to the high level required

There would appear in general to be substantial agreement upon the broad principles which should govern the basic training of the surgeon as well as upon the more technical phases of the postgraduate years. These ideas, principles and discussions may be said to have been largely responsible for the initial action taken by this association three years ago which led to the formation of the American Board of Surgery. If, however, the efforts of that Board and the splendid support which it has received from the surgical profession are to achieve the desired results, we surgeons must all of us give serious thought and untiring effort to the elevation of hospital standards to a level adequate for such training. This is specifically the obligation of the leaders of American surgery, and if they do not do it, it will not be done or at best will be poorly done. They must assume the responsibility for the elevation and maintenance of the standards of hospitals so far as surgery is concerned and must not allow it to be determined by our legislatures, state or national.

It is, therefore, very important that we immediately give serious attention to the problem of our hospitals, which, in the last analysis, with their wards, operating rooms, outpatient departments and laboratories, are where the young medical man of today must be trained to become the surgeon of tomorrow.

Is it not proper and fitting that surgeons as a group should be the most interested and responsible members of the hospital staff?

Practically speaking, the essential original incentive for the development of hospitals came from the need of a place properly organized and equipped for surgery. In the early days most of a hospital's activity was connected with surgery, at a time when the other branches of the medical art were largely practiced in the home.

The demands of surgery and the financial returns to the hospital from surgical patients are largely responsible for the remarkable development of hospitals which has taken place in this country since the birth of this association 59 years ago.

Since, therefore, we of the surgical profession have been so largely responsible for the development of hospitals and since we and our patients provide such a large part of the financial income of these institutions, should it not be our privilege, as well as our duty, to take an active part in the management and direction of the professional activities of our respective hospitals?

We know in general what the training of a surgeon should be and we are the only really competent persons to direct that training and to determine to a large extent what should be the hospital's attitude toward that training.

Unless we recognize and adequately meet our responsibility, the training will be ineffective and we shall be derelict in our duty

It is, I think, obvious that today we are living in a bureaucratic era, and it is my firm belief that the same bureaucracy, which most of us deplore, is gradually taking control of our hospitals, for even medical men are not altogether immune from this infection

We medical men are not, by and large, good business men. As the financial structure of our hospitals has become larger and more complicated, the business man has played an increasingly more important rôle. As long as he has devoted his attention to the financial and business management, he has, on the whole, been of great assistance

There is no occasion for any conflict between the lay group and the professional group if each will recognize and respect the knowledge and experience of the other. If, however, medical men in general, and surgeons in particular, are not on their guard they will soon cease to play the important part they should in hospital management

Sooner than we may wish government, local, state or federal, will be called upon to greatly increase their contributions to the support of hospitals and with this will come an increasing participation of government officials in hospital administration and, if we are not prepared to guide and direct them, an increasing control of professional matters

The most effective way to avoid this undesirable result is for us to take an ever more active interest in determining the policies and directing the professional affairs of our hospitals. To appreciate the dangers ahead of us is to be prepared to successfully meet them

The layman has his sphere in hospital management and the professional man has his. The "no man's land" between these spheres is where both groups should seek a harmonious solution of their mutual problems

Another of the most important hospital problems of the moment is the development of a true spirit of efficiency and economy. While a surgical department is, as a rule, a hospital's most important source of operating income, it is also a hospital's most costly activity. Hospitals in general, and surgical departments in particular, are both extravagant and wasteful, not from intent but because in our hospital relationships from third or fourth year medical student to chief of the Surgical Service we have never been taught to be or compelled to be economical. The practice of economy is never of sudden or spontaneous development but is rather the developed habit of a lifetime, a habit possessed to a remarkable degree by our forefathers but conspicuous by its absence in the American life of today

As elder surgeons, it is our duty to see that economical principles and practices are instilled into the minds of the young from the early days in the medical school so that later on they will become the habit of their professional lives

There is not a surgical department in any hospital in this country today in which there is not a large amount of waste of time, materials and the many

other items which make up the cost of maintenance of the department. The surgeon and the nurse are the outstanding ones who can effectively control this wasteful tendency and this can be accomplished by the development of an economic conscience in everyone who participates in the operation of the surgical department. How many of the costly whims and gadgets with which surgical departments are burdened are of any practical value? Simplification rather than complication of surgical procedure should always be our aim. Efficiency goes hand in hand with economy and true efficiency always means economy. It has long been my thought that the watchwords of a hospital should be efficiency, economy and most important of all—humanity, and who better than the surgeon can teach and practice this triad of virtues?

Another most important phase of hospital activity should be the development of a teaching atmosphere. This, of course, does already exist in a relatively small number of hospitals, especially those intimately connected with medical schools, but it does not exist in the great majority of hospitals throughout the land. Unless this teaching responsibility is recognized and the opportunities provided, how can adequate training for the surgeon of the future be had and where can young men secure the training and experience to render them eligible for the hall-mark of surgery which the American Board of Surgery proposes to place upon them?

In addition to those hospitals which already afford adequate facilities for such training, there should be many more such institutions in the near future scattered over our country. What a boon this would be to both the public and the profession and what a stimulus to the thousands of other hospitals to advance their standards. This, it seems to me, is largely the duty of American surgeons and especially of the members of this Association who in their hospital relationships represent many more than the number of adequately equipped hospitals needed today to train the surgeon of tomorrow.

From the latest report of the Council on Medical Education and Hospitals of the American Medical Association it would appear that there are only 44 hospitals in the United States which offer surgical services of three years or more. From this report it is impossible to determine in how many of these 44 hospitals the so-called intern year is included in the three years or more, but it is probable that it is included in a considerable number. This indicates how inadequate at present the surgical service in all but a comparatively few hospitals is, to give the training now required by the American Board of Surgery.

Concerned with our immediate problems of the moment, are we, as the leaders of American surgery, sufficiently aware of our duties and responsibilities for the future, so that when the torch passes from our hands it will be grasped by men better prepared than we to carry it on to their successors? Are we not devoting too much of our thought and energy to our specific personal interests and too little to the institutions we serve?

Closely associated with the foregoing, as one of the most important hospital problems, is the education and training of the nurse. Of all the groups

of medical men, surgeons are the most dependent upon the nurse, and it, therefore, behooves us to take an active part in the determination of what should be the education of the nurse

Very important changes are being made in the basic education of the nurse, many of which are excellent and many are not. The great danger to nursing as a profession today, in my opinion, is that its direction and control are largely in the hands of women of great crusading zeal whose minds are filled with fine theories but who often do not possess the practical knowledge and skill required for the training of efficient nurses. The possession of a so-called degree in nursing is certainly no guarantee of, or substitute for, a practical knowledge of nursing.

Many of the theories and some of the practices of the higher education for nurses have much to commend them, but these theories and practices need careful study and criticism and more than all else they need the constant direction of the medical mind and especially the mind of the surgeon.

In general, it is assumed that the nurse works under the direction of the medical man who is at least supposed to know something about her function and should have an active participation in her education, which he certainly does not have at this time.

Admirable as may be the efforts leading toward a higher education for nurses, what we surgeons, as well as medical men in general, need is women well trained to give adequate nursing care to the patient, and it certainly does not require four or five years to give such training.

It has been my observation and experience that the quest for so-called degrees in nursing does not improve the quality of the service rendered but tends to make the possessor of such a degree less efficient in the duties of the trained nurse and less qualified to impart the practical knowledge of nursing to her pupils. Her thoughts are too much occupied with educational themes and to little with the needs and care of the sick.

Unless we are on our guard, changes will be made in the education and practice of the nursing profession which will certainly not be helpful to the patient or the physician and of very questionable value to the nurse. The great danger is that the nursing mind, and the lay mind uncontrolled by the medical mind, will direct nursing education, with the result that the surgeon will have to take such nursing practice as is given him and try to like it. It is, therefore, very important that we surgeons take more active interest in the direction and control of nursing education and management in the hospitals with which we are connected.

Hospitals and their management are primarily and essentially the problem of the medical man and we should gladly accept this responsibility. There is no reason why the medical man should have a single track mind, and every reason why his mind should broaden to grasp and solve the professional problems having to do with the institutions in which most of his life is spent and most of his activities employed.

As professional men we should make every effort to preserve our liberty

of speech, thought and action and to resist the tendency to an abridgment of these liberties, no matter from what source it may come. This can best be accomplished by taking an ever active and unselfish interest in the management of the professional affairs of the hospitals and teaching institutions with which we are associated. Unless we exert ourselves, we shall certainly find the control and direction of our hospitals passing more and more into the hands of others less well qualified.

Enough has been said and written by administrative officials in Washington to indicate that their thoughts and plans are focusing on national regimentation of medicine. In peace as in war it is an old axiom that a sound offense is the best defense. In hospital affairs, as in national affairs, we should endeavor to be a self-governing people rather than a governed people.

The leaders of American surgery have for a long time believed that there should be some more distinguishing evidence of the ability to practice surgery than the mere possession of a medical degree. It was also fully realized that such standards of the ability to practice surgery should be determined by the profession and not by state or national legislatures. It was the crystallization of this sentiment which led to the formation of the American College of Surgeons some 25 years ago. It was believed that adequate training of the surgeon was an absolute necessity, but it was also appreciated that proper opportunities for such training must be provided. This resulted in an effort to survey and standardize the hospitals of the country, coupled with an untiring effort to raise hospital standards in the interest of the patient and also in order that better facilities for the training of the surgeon might be provided.

For many years inspection and grading of hospitals has been carried on more or less independently by the American College of Surgeons and the American Medical Association. This inspection has brought about a marked improvement in hospital standards and hospital service.

The Hospital Associations are also very much interested in this work and have given valuable assistance. There would appear, however, to have been a duplication of effort in these activities and it would certainly be of great advantage if all these activities could be combined under the cooperative guidance of one group composed of representatives of the most important associations concerned. This group in its activities and accomplishments could do for the elevation of hospital standards the same kind of effective work that the Council on Medical Education of the American Medical Association, the Association of American Medical Colleges and the State Medical Boards have done for the standards of medical colleges. Both the American College of Surgeons and the American Medical Association have in existence, and in function, not only most of the set-up required but also the nucleus of the personnel.

I think there will be general agreement that at the present time the surveys of hospitals are far too cursory and incomplete to allow of adequate and accurate grading. To properly survey a hospital requires qualities that are

acquired only by experience, and great care should be taken in the development of an efficient personnel. Such ability should command adequate salaries so that the turnover of the personnel would be as limited as possible. Such investigators of experience would be of the greatest assistance to hospital managements in advising wherein lay their defects and how best to correct them.

Inspection of all hospitals should be made at regular, and not too infrequent, intervals and gradings rearranged as conditions determined. The whole system of hospital inspection and grading needs revision and amplification, in fact this would appear to be one of, if not the most, urgent need of the hospitals of this country.

Unless some such effective organization as this can be brought into existence to function fearlessly, the problem as to where the surgeon is to be trained cannot be properly solved, and the effort to improve the training of the surgeon and to give him the mark of distinction conferred by the American Board of Surgery will fall far short of our anticipation.

To anyone familiar with the subject it is very evident that there is a complete lack of any basic standard for graduate training in surgery and it is equally evident that there is an imperative need for the formulation and adoption of some such basic standard as soon as practicable.

We must not only have more hospitals in this country so organized that the necessary training of the surgeon can be given, but there must be some way of knowing just what and where these hospitals are, so that the young man desirous of securing such training will know where to go.

While these remarks have been directed particularly to the problems of the surgeon, they are also in a great measure the problem of all branches of medicine, and it would seem reasonable to expect that some such cooperation as suggested would receive the general approval and support of the medical profession.

As a result of a careful study of the present incoordinated and overlapping activities of different groups, the suggestion has been made by Dr. Willard Rappleye, Dean of the School of Medicine of Columbia University, that a National Council on Medical Education be created, to be composed of representatives of the universities, medical schools, hospitals, practicing profession, specialty boards, state licensing bodies and public health agencies.

The functions of this proposed National Council on Medical Education would be those of studying the major educational needs of American medicine and of formulating adequate standards for these activities. Such a National Council could be of the greatest assistance in advising and directing the many agencies having to do with the health program of the nation.

Under the direction of such a National Council the problem of hospital grading and standardization could and would be more effectively solved since the organizations already having that important matter in their hands would have a better understanding of the real educational needs in each specialty field.

The creation of this Council must appeal to everyone as being the most practicable solution yet proposed for this intricate problem.

In brief summary an effort has been made to emphasize

(1) The need of immediate efforts to provide adequate facilities for the training of the surgeon

(2) More active, unselfish interest on the part of surgeons in directing the professional affairs of the hospitals with which they may be associated

(3) The establishment of harmonious relationships between the professional group and the lay group in directing hospital activities

(4) The development of a teaching atmosphere in hospitals

(5) The need for and importance of efficiency and economy in hospital activities

(6) The careful supervision and direction of nursing education by the medical profession

(7) The imperative need of more careful inspection and accurate grading of hospitals

It is quite beyond the scope of such an address as this to attempt to solve the problems which have been presented. All that can be done is to direct attention to them in the hope that the recognition of their importance and implications will be an aid in their solution.

THE NEED OF A NATIONAL COUNCIL ON MEDICAL EDUCATION, LICENSURE, AND HOSPITALS

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It is a great privilege to be permitted to present to you certain considerations bearing upon medical training and practice. Probably at no time in our history have there been greater opportunities for leadership and guidance of public policies relating to medical questions. It is generally agreed that the essential feature of an adequate program of health services is a sufficient number of competent physicians. Upon medical education broadly conceived rests the responsibility of recruiting and training such personnel and of providing opportunities for practitioners to keep abreast of new knowledge and methods of diagnosis, treatment, and prevention.

A large number of separate organizations are dealing with different features of the whole problem, some of them with conspicuous success in their own spheres of influence, although a great deal of duplication, overlapping, competition, and confusion exists. At the same time there are important needs that no individual agency is covering satisfactorily and for which no organization feels responsible. It is of great importance that a thoughtful appraisal be made of our present efforts to meet the current needs and the impending demands upon the profession, and that we be prepared at least to consider ways and means of adapting our existing programs to meet more effectively the responsibilities which are likely to be placed upon us in the future.

Because of the special conditions in the early days of American medicine, the three functions of medical training, practice, and licensure were vested in the practicing profession. This was in contrast with the situation even at that time in most of the continental countries of Europe where for centuries medical education was the responsibility of the universities and licensure to practice was a function of the state. In Great Britain and France professional training was largely developed in the hospitals, with licensure resting in the agencies of the state. It is true that in this country there were some medical schools of high standing but most practitioners of 100 years ago had been trained by the apprenticeship method.

The historical background and tradition in this country of the control of medical training by the profession explains some of the present confusion and difficulties. Medical training now, however, has become the responsibility of medical schools, which are usually associated with universities. All students today must have a period of college preparation preceding the professional training, nearly every graduate takes a hospital internship, every state has its own agency for licensure, the new nationwide plans for graduate and postgraduate education involving the cooperation of the medical schools,

hospitals, and the profession have been instituted. These developments have occurred in segments and sometimes without much relationship to other parts of the whole structure of medical education or to the programs of other agencies carrying out parallel or duplicating activities.

Only a few items of recent history need be mentioned to suggest the various directions and many sources from which contributions have been made to our present standards of medical training. Just before the Civil War, most states by legislative action had removed the function of licensure from medical societies and had placed it under state boards of examiners. Much of this legislation was repealed at the time of the War. About 1870, agitation was renewed for the licensing of physicians by the state, largely because of the recognition of the dependence of sound clinical medicine and practice upon the discoveries in bacteriology, pathology, physiology, and the other sciences. By 1895, practically every state had created some kind of legislative organization regulating medical training and the examination and licensing of doctors. The legal enforcement by the different states of proper standards of training for licensure to practice has been one of the most important factors in elevating medical education in this country.

During the period mentioned above other important developments had occurred. The Association of American Medical Colleges was organized in 1891 to coordinate the educational efforts of the stronger medical schools. In response to the rapidly growing scientific content of medical training, Harvard University, in 1892, increased the length of the course to four years. A number of other schools promptly adopted similar programs. The founding of the medical school of Johns Hopkins University, in 1893, further stimulated the awakening interest in medical education.

In 1899, the graded curriculum for medical instruction was adopted generally in this country. At about that time the American Medical Association began its important work of collecting and publishing statistics on the medical school situation. In 1904, it created the Council on Medical Education which is responsible to the House of Delegates elected by the state medical societies. In 1909, that Council adopted as its standard the four year course which was in force in most of the leading schools at that time. Seventeen medical schools had already established the requirement of two or more years of college work for admission and 11 more made that regulation effective in 1910. This requirement was embodied in the minimum standard of the Council eight years later, at which time 81 of the 90 schools then in existence had adopted that requirement. It happens that eight states do not yet officially require two years of premedical college preparation although most of these states admit to their licensing examinations only graduates of approved medical schools. The monumental study by Mr. Abraham Flexner for the Carnegie Foundation for the Advancement of Teaching was published in 1910. That study and the publicity it received gave great impetus to the efforts to establish high standards of training and stimulated the needed financial support for medical education and research and for teaching hospitals.

Full credit is due to all the different individuals and organizations which contributed to the rapid elevation of the standards of medical training in this country, particularly to the courage, leadership, and financial aid of the universities and educational foundations, the participation of hospitals in the teaching plans, and the enforcement of standards by the state boards. There is no need of reciting here the contributions of the American Surgical Association and of the American College of Surgeons to the training and practice in surgery and the striking influence you have had on hospital standards in this country. The Association of American Medical Colleges and the universities have devoted great energy to the improvement of the basic undergraduate course. The Federation of State Medical Boards, individual state boards, and the National Board of Medical Examiners have rendered invaluable aid in their respective fields of action. The hospital associations are assisting in every way and now have greatly enlarged problems because of the newer demands upon them for better intern training and for graduate programs. All of you are familiar with the plans of the 12 American boards and of the Advisory Board for Medical Specialties which are largely responsible for the rapid and sound progress in graduate training. Special credit should be given to the Council on Medical Education and Hospitals, particularly in dealing with the proprietary, commercial, and weaker schools and in the collection and distribution of data on students, schools, state board activities, and other features of the whole program. While rules, regulations, and minimum standards have played an important part in the evolution of the present programs, the great strides have been made at levels well above the minimum standards by individual schools and universities under local leadership and by the desire of other institutions to emulate their successful undertakings.

As a result of the activities described and the increasing necessity of medical schools to provide adequate training in the medical sciences, which could not be met either by the weaker schools or by the commercial and proprietary institutions, the number of medical schools in the United States was reduced from 154 four year medical schools, in 1906, to the present 67. The graduates dropped from 5,364, in 1906, to 2,520, in 1922, but there has been a marked increase since that year. The number reached 5,377 in 1937, a total almost identical with that of 1906. In other words we are today graduating as many physicians from 67 medical schools as we did from 154 institutions 32 years ago. That a number of schools have enrolled more students than they can educate in keeping with present day standards has been recognized for years. During the last three years, however, the entering classes of certain of the schools have been reduced. In time the size of the student body in some of the institutions will be better adapted to their educational facilities and teaching programs. The figures cited do not include the additions to our profession annually from Canadian and foreign sources, from unapproved institutions, and from Americans who study abroad.

It is common knowledge that, despite efforts of the last 30 years to standardize medical education, "wide differences continue to exist in buildings,

equipment, personnel, students, financial support, hospital facilities, and educational policies" In response to this situation a reinspection of the medical schools made recently by the Council on Medical Education has shown that about 20 of the institutions approved by that Council do not even now provide a fully satisfactory preparation. If it is true, as stated by the Commission on Medical Education, that "an emphasis on educational principles in medical training and licensure can be secured only by modifying the point of view and broadening the interests of those responsible for medical education and licensure, not by recommendations, statistics, new regulations, further legislation, or manipulation of the curriculum," the evaluation of medical school objectives and programs can best be secured not by an agency representing the profession alone, which really is the alumni body of the schools, but by one which represents fully as much the educational, hospital, licensing, and other phases of this problem.

Students entering medicine prepare in about 600 colleges and universities. The requirements for admission vary considerably. There is a wide range of opinion on the objectives and content of preprofessional education. The basis of selection by different schools is not only undefined but frequently contradictory. Recent developments in graduate fields of instruction emphasize the need of better criteria of selection at the source. The situation is confusing to students and to those responsible for the conduct of the colleges and universities. There are numerous problems relating to general and medical education pressing for study and solution, yet there is no convenient mechanism in existence by which these mutual problems of medical schools and colleges can be discussed and defined.

The increasing dependence of sound medical education upon individualized, supervised experience in the teaching wards and clinics by means of the clinical clerkship presents special problems for the hospitals. The internship has become universally recognized as an essential part of the basic preparation for practice. Twenty states now require such a training for admission to the licensing examinations. Certain of them so define and regulate this period of training, however, that they defeat the efforts of universities, medical schools, and hospitals to provide a satisfactory preparation adapted to the needs of those going into different fields of practice. Uniformity, rigidity, and regulation are not distinguishing characteristics of an educational program. It is well known that the intern period is poorly adjusted in many hospitals to the preceding medical course, to the needs of the student, and to subsequent graduate training. Even the approval of national evaluating bodies is uncertain. An intensive study of internships in a group of eastern hospitals recently has shown that not more than a half of those hospitals approved for intern training by the Council on Medical Education and Hospitals provide satisfactory educational standards. The proportion of residencies meeting a real educational level is smaller. There is need for joint and continuing study of the place and functions of the internship and

residency in the evolution of the medical course, graduate training, and licensure

Excellent cooperation exists between most of the state medical boards and the medical schools and between the large majority of the different states on matters of reciprocity and indorsement of educational credentials. The National Board of Medical Examiners, organized in 1915, has been very helpful in establishing a national point of view regarding licensure. Many believe that medical licensure in the country as a whole could be simplified through some joint action by the Federation of State Medical Boards, the Association of American Medical Colleges, and the National Board of Medical Examiners. It is reasonable to assume that eventually this problem will be dealt with in a manner analogous to that found satisfactory in other countries. At the present time no agency exists for study and integration of this important public and educational function.

Plans already developed for graduate and postgraduate training will require wide and, in some instances, fundamental readjustments in hospital services, if the hospitals are to participate fully in these newer opportunities. The medical schools and universities are being called upon to assume responsibilities in these same programs. All are being subjected to numerous surveys and inspections by different agencies, frequently overlapping in their interests and conflicting in their objectives. The 12 American specialty boards and the Advisory Board for Medical Specialties, created in 1933, recognize the dangers of rigidity, regimentation, and regulation in the field of graduate training which must depend so largely upon the educational initiative, self-reliance, and resourcefulness of the individual. The upward extension of medical education into the graduate fields should be based, with necessary adaptations, on those principles of selection of students, concepts of learning, forms of instruction, and other features which characterize true graduate education.

Sound plans for the evaluation and approval of graduate programs cannot be evolved by a single agency but call for cooperative action by a group representing the various major interests involved. The proposals, for example, that national and state registers or directories of specialists be created and that general practitioners be certified for continuation instruction have definite relationships to present methods of licensure. The state agencies should obviously be brought fully into the general plan.

The premedical student, the medical student, the intern, the hospital resident, the general practitioner, the specialist, and the public health administrator should be regarded from an educational point of view merely as different phases of the training of personnel to meet the health needs of the country. The problems from college preparation to retirement from professional life should be looked upon as parts of a single educational program. Portions of the program are primarily within the jurisdiction of universities, some are largely within the domain of the hospitals, others are in the various fields of practice, and some are under governmental regulation.

It is becoming increasingly apparent to those familiar with the situation that there is need of coordination of the various phases of medical education and better definition of the several areas of responsibility of national and state agencies, universities, hospitals, and professional bodies dealing with portions of the whole program, if medicine in this country is to meet fully its obligations. Reluctant as one may be to see another agency in medicine, the logical conclusion from the present more or less unrelated and frequently overlapping efforts is to create a national coordinating body representative of the major activities in medical education and service in order more effectively to meet the new conditions and needs of the country.

A National Council on Medical Education, Licensure, and Hospitals should be created from within our present organizations, made up of representatives of the universities, medical schools, hospitals, practicing profession, specialty boards, state licensing bodies, and public health agencies. There should be no difficulty in securing full representation of leaders in every subdivision of medical education and practice, hospital activities, licensure, and public health on such a central body. If such an organization is created the modest financial support from voluntary sources should not be difficult to obtain.

The functions of the proposed National Council on Medical Education, Licensure, and Hospitals would be those of studying the major educational needs of American medicine, of mobilizing the best current opinions regarding the different phases of professional training at its several levels, of formulating adequate standards for these activities, and of advising regulatory bodies and governmental agencies on standards, methods, procedures, and areas of action. The National Council should, among other things, delegate to existing organizations all administrative functions and endeavor to coordinate the efforts and simplify the procedures of the multiple agencies now in operation. A central clearing house carrying influence and prestige by virtue of the knowledge and judgment of its personnel and providing a suitable vehicle of our own creation for cooperation on matters dealing with all features of medical education, transcending the activities and interests of any single group or organization, would be of the greatest practical value to the profession, the universities, the hospitals, the licensing bodies, and the future health program of the entire country.

DISCUSSION—DR EVARTS A GRAHAM (St Louis, Mo.) I think that Doctor Rappleye has unquestionably put his finger directly on a great need which exists in this country and which has existed for a long time.

Some of you may think that the functions of this proposed Council are already being carried out to a considerable extent by existing organizations, as, for example, the Council on Medical Education of the American Medical Association. That is hardly correct, however, because the Council on Medical Education of the American Medical Association, for instance, is a body which really represents only the American Medical Association. It is not representative, at least so far as appointments are concerned, of the medical schools of the country, the universities and the various other elements which Doctor Rappleye mentioned in his paper.

Despite the fact that, as has been mentioned by the President in his address

and has been intimated by Doctor Rappleye in his paper, we are living in a bureaucratic age, despite that fact, it does seem as if it would be desirable and necessary to have another council set up which, however, I would infer from Doctor Rappleye's paper, would not have any direct authority allocated to it except an authority of prestige. Perhaps he will make this point a little more clear in his closing remarks.

Certainly there is a danger in too much standardization of education in any form. There would be a danger in setting up a body which would have a thorough standardization, that is to say, a legal authority, perhaps, to tell the medical schools exactly what they should do and exactly what they should not do. This probably would be destructive of the very principles of sound education.

We have seen in recent years in Europe too much of this tendency to wish to welcome it here in the United States. I am quite sure, from talks with Doctor Rappleye about this matter, that he does not mean that this council which he proposes should have any such Fascistic power as some might fear for it.

There is no question about the fact that there is a need of a coordinating body to coordinate all of the activities and functions of the various independent bodies, which now exist in a large number in this country, all attempting to aim at the same goal, more or less, but missing that mark to a considerable extent because of duplication of effort, because of failure sometimes to grasp the essential point in the strategy of the whole campaign, and because too often the emphasis is placed on the details rather than on the fundamental principles involved.

Actually, of course, the most important and the most fundamental cog in the whole machine of the care of the sick is the doctor. One of the most important elements in the matter of how good a doctor is or how poor and ineffective he is, is the question of the training of that doctor, his education and the facilities which are offered to him to keep abreast of developments which have taken place in medicine since the time that he left the doors of his medical school.

Any plan of improvement of the care of the sick on a large scale which does not take into serious consideration, as one of the most fundamental steps necessary, the improvement of the educational facilities for the practicing doctor will, of course, fall far short of its goal.

We read in the newspapers a few months ago about a recommendation, for instance, which had been made to the national government that small hospitals—the newspaper account which I read stated hospitals of 30 to 60 beds—should be erected throughout the country in order that the isolated sick in the rural communities could be taken care of properly, rather than to undergo the hardships of being taken care of in poorly equipped homes.

It is easy, of course, for anyone who knows what the practice of medicine is all about to realize immediately that if the country should become studded with hospitals of 30 to 60 beds, serious effects would result, which would be, in the first place, that these hospitals would be in competition with the large private hospitals throughout the country, which have had a splendid record in unselfish training of the medical profession to go out and take care of the sick. It would mean that these small hospitals are totally inadequate themselves to provide proper facilities for the responsibility of training doctors. It would mean, therefore, that probably in general, the public as a whole would suffer from such a plan instead of being improved by it.

I take it that the function of such a council as Doctor Rappleye has in mind would call attention to such a serious defect, for example, in such a proposal,

and with the weight of prestige behind it, as containing representatives of various important bodies, would perhaps have enough influence to curtail efforts which might be made from time to time by well meaning individuals to propose schemes for the welfare of the sick which actually would not be practical, and would present such defects as those I have just mentioned in regard to this particular instance

There is really nothing new about Doctor Rappleye's proposal, as he has indicated. It happens merely that we in the United States have been slow to put such a measure into operation. I believe I am correct in saying that the British Medical Council, which has been in existence for nearly 100 years, has been and is an organization which carries on many of the functions which Doctor Rappleye proposes, for example, for this Council, the formation of which he advocates. Perhaps he will elaborate on that a little more in closing his discussion.

Finally, Mr. President, I should like to ask Doctor Rappleye what he wishes to do about this. I am not quite sure whether he wishes a resolution of some kind from this Association, expressing approval of the creation of such a National Council, or whether he merely wishes to think about this matter for a while and perhaps some time later discuss it again. I should like, Mr. President, to ask you to ask him, if you will, whether he wishes the American Surgical Association to do something about it.

DR HAROLD L RYBINS (New York State Board of Medical Examiners) I think the best light I can throw on Doctor Rappleye's very important contribution is to draw attention to the fact that within the last 10 or 15 years, there have been at least half a dozen sporadic movements in exactly the direction that he is pointing out now, and that all of these movements have come about through the necessity for the expression of opinion and sometimes of action from various representatives of all interested parties in medicine.

For example, all of you are familiar with the fact that the National Board of Medical Examiners, which has been functioning now, I think, for about 20 years, has representatives in practically every interested medical organization throughout the country. It has just dawned upon me what a monumental piece of politics and strategy that Board has accomplished in actually taking over some of the functions of 40 odd governmental agencies without the least amount of bad feeling.

It has accomplished something which none of the individual boards could ever have accomplished, and it has done so by taking some of the functions of those boards away, and still there has been absolutely no friction between the state boards, which are governmental agencies, whose members are mostly appointed by governors, and the National Board.

The answer is this. Apart from the very great political skill of Doctor Rodman and his associates, the Board has had such a broad representation in its make-up that there could be no question of its prestige and of its public interest. The fact that it has been able to accomplish what it has is a very good indication of what a National Council, such as suggested by Doctor Rappleye, might do without any friction whatsoever.

About 10 years ago, it became apparent that we ought to know something more about medical education, therefore, a Commission on Medical Education was formed. This, again, was made up of representatives of practically every organization in the country interested in medical education. No administrative function was assumed in this case. Simply, a study was made and a lot of facts were collected. There was some deliberation upon these facts and a report was finally made which contained very vague, if any, recommenda-

tions Nevertheless, the effect of this Commission was exceedingly far-reaching upon the advance in medical education in this country In fact, it was more far-reaching than any more specific regulations and laws that had been heretofore laid down as to how to conduct medical schools

As far as I know, there was no serious friction between the Commission on Medical Education and the various interested bodies

We are at the present time in the throes of organizing a Commission on Graduate Medical Education, which we hope will operate in exactly the way that the earlier Commission did, and which will bring together some information and some ideas about graduate medical education which none of the present existing agencies seem to have been able to bring to the attention of the public

Again, about seven or eight years ago, a very serious problem arose, when it was suddenly discovered that a very large number of American boys who were able to gain admission to foreign medical schools were studying in Europe with the expectation of returning to this country to practice This problem was brought to the attention of the various individual bodies concerned from time to time, but no one of them seemed able to cope with the problem Finally, the numbers increased to something over 2,000 a year, and the situation became so acute that it became necessary to form a Joint Committee on Foreign Medical Students which could represent the interests and speak for all the various bodies concerned

As soon as we had one committee which had authority to speak for everyone in American medicine and American licensure and American hospitalization we were able to deal very adequately, and simply, with the representatives of the European governments, but no one single agency would have been able to do so

Then again, during the last 15 years, at least, there have been developing, as you know, the various boards for medical specialties, but in spite of the fact that several of them were very well organized, no one seemed to be able to work out a program which would smooth over the difficulties between the various boards—the difficulties arising between those boards and the organized medical profession

About four, certainly not more than five years ago, it was deemed advisable to create an Advisory Board of Medical Specialties which was to be made up of representatives of all the interested bodies, and which was to interject itself between the medical profession as organized and these individual bodies as organized The result of this interjection by this broadly organized group has been the complete organization and, as you know, operation of the 12 specialty boards which are deemed to be desirable at the present time

I think there is no question that had there been no advisory board which could speak for all the interested bodies, there would still be an amount of unnecessary jangling between the individual boards and between the individual boards and organized medicine as a whole

I bring these facts to your attention I might also mention the survey of medical schools which Doctor Rappleye spoke of and in which there was some cooperation between the Council, the Medical Schools Association and the Federation of State Boards

I bring these six points to your attention (and I believe many more could be recited) to show that during the last 15 or 20 years, the need has arisen for some sort of National Council with a broad representative base, and the prestige that comes from such representation, to meet the problems of mutual

interest that are always developing Within the last 15 to 20 years, we have had at least six such occasions

Now, if the government in Washington is going to continue as actively as I believe it is, I believe seven or ten occasions will arise very shortly, and I agree with Doctor Rappleye that it is very much in the interest of the medical profession, and even more in the interest of the public health, that there be a genuinely representative organization that can speak with intelligence and authority for the entire medical profession and the lesser individual bodies, whose important functions should certainly not be interfered with

DR WILLARD C RAPPLEYE (closing) Doctor Graham brought up the question of authority, and he is quite right in interpreting what is certainly in my own mind, and I think in the minds of most of the persons who have been thinking about this problem and seeing the situation develop, that we are concerned primarily with getting together a group of persons who will represent the leadership of ideas and carry with it the prestige and weight of authority that would arise by having real judgment on a great many of these interlocking problems

We are all prone, of course, to think of our own situations and problems, and I think we need some agency that is extending over and above the interests and responsibilities of single agencies as we now have them, many of which are doing excellent work in their respective fields The whole idea back of the proposal is to make progress at the top as well as at the bottom Leadership is going to be always at the top

There is no question, and the fact remains obvious to everyone, that the government is involved in the program of medicine and is going to become a great deal more so It seems to many of us that we ought to become organized in advance and be prepared to give that authoritative advice and counsel that it ought to have I am not sure that they will take it all the time, we don't expect that, but certainly we have to be in a position, at least, to have some mechanism set up within the profession to help in guiding many of these problems that cut across all of our national agencies, hospitals, medical profession, licensing bodies and similar activities

The question of the General Medical Council Those of us who have been interested in the history of that organization, and other plans of medical education and licensure in other countries, have been very much struck with the fact that the situation in this country, at the moment, is almost identical with that leading up to the organization of the General Medical Council, in 1858 We have similar problems Many of the situations that we have today are closely paralleled with those that led to the formation of the General Medical Council

I would like to speak about what Doctor Rypins has said He has brought out the very point that this technic of cooperation between the agencies is going on and there are a number of activities already set up, many of them temporary, that have gone forward with the idea of formulating joint programs that have a bearing on medical training

This is not a radical suggestion It was embodied in the report of the Commission on Medical Education to which Doctor Rypins referred, which was printed in 1932 It is only following along what has been going on for the last 100 years in medical education in other countries, and in recent years in this country

THE TREATMENT OF CRANIAL OSTEOMYELITIS AND BRAIN ABSCESS

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SUPPURATIVE lesions of the scalp, skull, accessory sinuses meninges and brain bear an intimate relationship to one another since the infection may spread by contiguity or travel along lymph and diploic channels, and along emissary veins which communicate with veins that pass through the dura into the substance of the brain. Appropriate surgical treatment of the localized infection often will limit its extension and prevent the more serious involvement of the meninges and brain.

The treatment of osteomyelitis of the skull does not differ from the treatment of osteomyelitis of other bones, removal of all necrotic and infected osseous tissue is required in addition to sequestrectomy. However, special consideration concerning these operative procedures is necessary, since the scalp and periosteum may have been destroyed, and removal of infected bony tissue may result in exposure of the meninges, moreover, brain abscesses are frequent sequelae of osteomyelitis of the skull.

A consideration of the anatomic arrangement of the veins in the diploe and of the emissary veins is in order, so that it may better be understood how infections may travel through communicating veins to give rise to distant areas of osteomyelitis, with or without accompanying brain abscess. Infective emboli in the arterial system are rarely responsible for osteomyelitis of the skull. Thrombosis of vessels in an extending infection of the scalp frequently spreads the osteomyelitis. The arterial supply to soft tissues and haversian canals about an osteomyelitic region serves as a barrier to limit the progress of infection by maintaining the life of the osseous tissue. Frequently, the osteomyelitic process will destroy but one table of the skull when the circulation to the opposite table has been maintained.

Gray²² states "The diploic spaces of the cranial bones in the adult contain a number of tortuous canals, the diploic canals (*canales diploici* [Breschet]), which are surrounded by a more or less complete layer of osseous tissue. The veins they contain are large and capacious, their walls being thin and formed only of endothelium resting on a layer of elastic tissue, they present at irregular intervals pouch-like dilatations, or culs-de-sac, which serve as reservoirs for the blood.

"In adult life, so long as the cranial bones are distinct and separable, these veins are confined to the particular bones, but in old age, when the sutures are united, they communicate with one another and increase in size. They communicate, in the interior of the cranium, with the veins and sinuses of the dura, and on the exterior of the skull with the veins of the pericranium. They

consist of (1) The frontal diploic vein (*v diploica frontalis*), which opens into the supraorbital veins by an aperture in the supraorbital notch, (2) the anterior temporal diploic vein (*v diploica temporalis anterior*), which is confined chiefly to the frontal bone, and opens into one of the deep temporal veins through an aperture in the greater wing of the sphenoid, (3) the posterior temporal vein (*v diploica temporalis posterior*), which is situated in the parietal bone, and terminates in the lateral sinus through an aperture at the posteroinferior angle of the parietal bone or through the mastoid foramen, and (4) the occipital diploic vein (*v diploica occipitalis*), the largest of the four, which is confined to the occipital bone, and opens into the lateral sinus or the torcular Herophili.

"The emissary veins (*v emissaria*) are vessels which pass through apertures in the cranial wall and establish communications between the sinuses inside the skull and the diploic veins in the diploe, and the veins external to the skull. Some of these are always present, others only occasionally so. They vary much in size in different individuals. The principal emissary veins are the following: (1) A vein (*v emissarium mastoideum*), almost always present, runs through the mastoid foramen and connects the lateral sinus with the posterior auricular or with the occipital vein. (2) A vein (*v emissarium parietale*) which passes through the parietal foramen and connects the superior sagittal sinus with the veins of the scalp. (3) A plexus of minute veins (*v rete canalis hypoglossi*) which pass through the anterior condylar (hypoglossal) foramen and connect the occipital sinus with the vertebral vein and deep veins in the neck. (4) An inconstant vein (*v emissarium condyloideum*) which passes through the posterior condylar foramen and connects the lateral sinus with the deep veins of the neck. (5) A plexus of veins (*v rete foraminis ovalis*) connects the cavernous sinus with the pterygoid and pharyngeal plexuses through the foramen ovale. (6) Two or three small veins run through the foramen lacerum medium and connect the cavernous sinus with the pterygoid and pharyngeal plexuses. (7) There is sometimes a small vein connecting the same parts and passing through the inconstant foramen of Vesalius, opposite the root of the pterygoid process of the sphenoid bone. (8) A plexus of veins (*plexus venosus caroticus internus*) traverses the carotid canal and connects the cavernous sinus with the internal jugular vein. (9) A small vein (*v emissarium occipitale*) usually connects the occipital vein with the lateral sinus or the torcular Herophili and the occipital diploic vein. (10) A vein is usually transmitted through the foramen cecum and connects the superior sagittal sinus with the veins of the mucous membrane of the nose."

OSTEOMYELITIS — *Etiology* Osteomyelitis results from infection of an avascularized bone or from extension of an infection into the diploic canals.¹⁷ The most common sources for the infection are contaminated, compound, comminuted fractures of the skull, furunculosis of the scalp and extension of infections from the ear and accessory nasal sinuses, the frontal sinus being the chief offender. Diffuse osteomyelitis of the outer table is more prone to

afflict children and young adults than is osteomyelitis of the inner table of the skull, since the outer table is more porous. *Staphylococcus pyogenes aureus* is chiefly responsible for osteomyelitis resulting from infections of the frontal sinus and is the organism which frequently produces the osteomyelitic processes in compound comminuted fractures, with infected, lacerated wounds.

The denuded skull, resulting from burns by electricity and fire, from extensive lacerations, and from removal of the scalp because of tumors, ultimately, undergoes destructive processes. If the circulation to the inner table is intact, only the denuded outer table will degenerate and separate as a sequestrum.³³

Craniotabes, gummatous osteomyelitis,¹ caused by syphilis, is a representative of the group of chronic infections. *Eberthella typhi* (*Bacillus typhosus*) at one time was a fairly common cause of osteomyelitis but today, since the introduction of vaccination, is rarely seen. An occasional case results from tuberculous involvement of the skull. Actinomycosis, too, occasionally is responsible for infective processes of the skull.

Pathology—The process of osteomyelitis begins with the introduction of suppurative organisms into the vascular channels of the skull. If the bone is denuded of its scalp, the process will extend until adequate circulation is encountered. Frequently, accompanying cellulitis will destroy the circulation of the scalp about the denuded bony area and this further encourages extension of the osteomyelitis. The seipiginous extension along diploic canals will give rise to additional areas of necrosis beyond the original focus.³⁵ The infection of diploic veins results in thrombosis and the development of granulation tissue. This process may extend either to the pericranial or to the intracranial structures by extension along emissary veins. Phlegmons of the scalp develop over the necrotic bony areas and extend the infection over suture lines to new areas, through emissary and diploic veins, thus giving rise to additional osteomyelitic processes.²⁹ The disease may progress until the entire skull has been involved. On examination of the skull, islands of normal bone will be found between necrotic and sequestered areas. These islands apparently have resisted the infection, owing to the fact that the circulation has been maintained and that a zone of granulation has served as a barrier in limiting the infection in the diploic canals.

The reparative process of granulation and absorption works in conjunction with the destructive process. As the bony cells die they disintegrate, are absorbed and are replaced by granulation tissue. This is readily demonstrated in a denuded area of skull. The exposed bone at first appears dry and dead-white, but sooner or later a zone, or ring, of granulation will appear at the scalp margin. In the zone of granulation there will develop a localized osteomyelitis which eventually destroys a ring of bone in the outer table of the skull. When this has taken place, the granulation tissue in the diploic spaces will actually lift from the dead-white outer table of the denuded skull (Fig. 1). Removal of the granulation tissue will reveal that the inner table is usually intact and is very vascular, owing to the fact that its circulation has been main-

tained by small arterioles from meningeal arteries. However, if the scalp has been destroyed by a severe burn, both tables of the skull will slough away spontaneously.

Symptoms—The local symptoms are usually preceded by a history of infection. If the symptoms follow injuries of the scalp and skull, a septic temperature of low grade develops, associated with leukocytosis and with localized swelling of a soft and doughy consistency, with or without localized tenderness. If the infection results from frontal sinusitis, the swelling will appear over the frontal bone, usually on the side of the involved sinus.⁷ When the infection is of hematogenous origin, as it is in syphilis, the swellings may

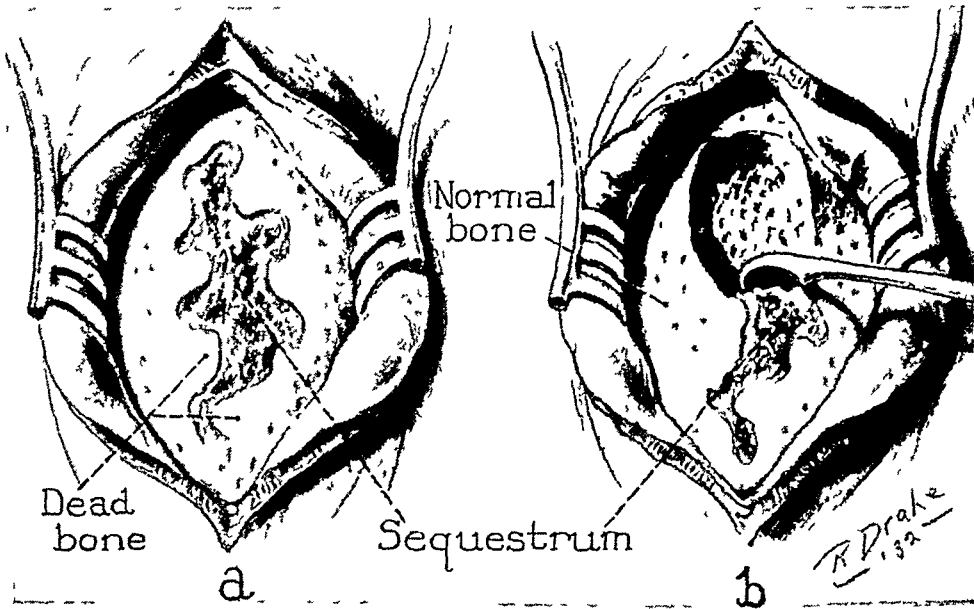


FIG. 1.—(A) Drawing showing worm-eaten erosions of osteomyelitis involving the outer table. (B) The procedure employed in removal of the sequestrum and the overhanging ledges of dead, white bone.

occur in numerous parts of the skull, but usually in those parts where the cranial tables are thickest, and where the diploic spaces are largest, as in the parasagittal portions of the frontal and parietal bones. Roentgenologic examination usually reveals moth-eaten erosions of one or both tables of the skull. All roentgenograms should be taken in two directions in order to demonstrate the extent of the lesions.

Surgical Treatment—The phenomena of destruction and repair form a basis for surgical treatment, since adequate drainage of suppurative lesions of the scalp, removal of infected bony fragments and removal of dead and necrotic bone will aid in preventing or limiting the osteomyelitic process.⁴ Small puncture-like incisions over fluctuating areas are of some value but are not sufficient surgical procedures to check the process. Localized osteomyelitic areas will continue to spread until the scalp has been reflected and all of the dead and sequestered bone has been removed. Frequently the necrotic bone can be removed with a sharp curet or gouge without removing both tables of the skull (Figs. 2 and 3). However, there is less danger of the

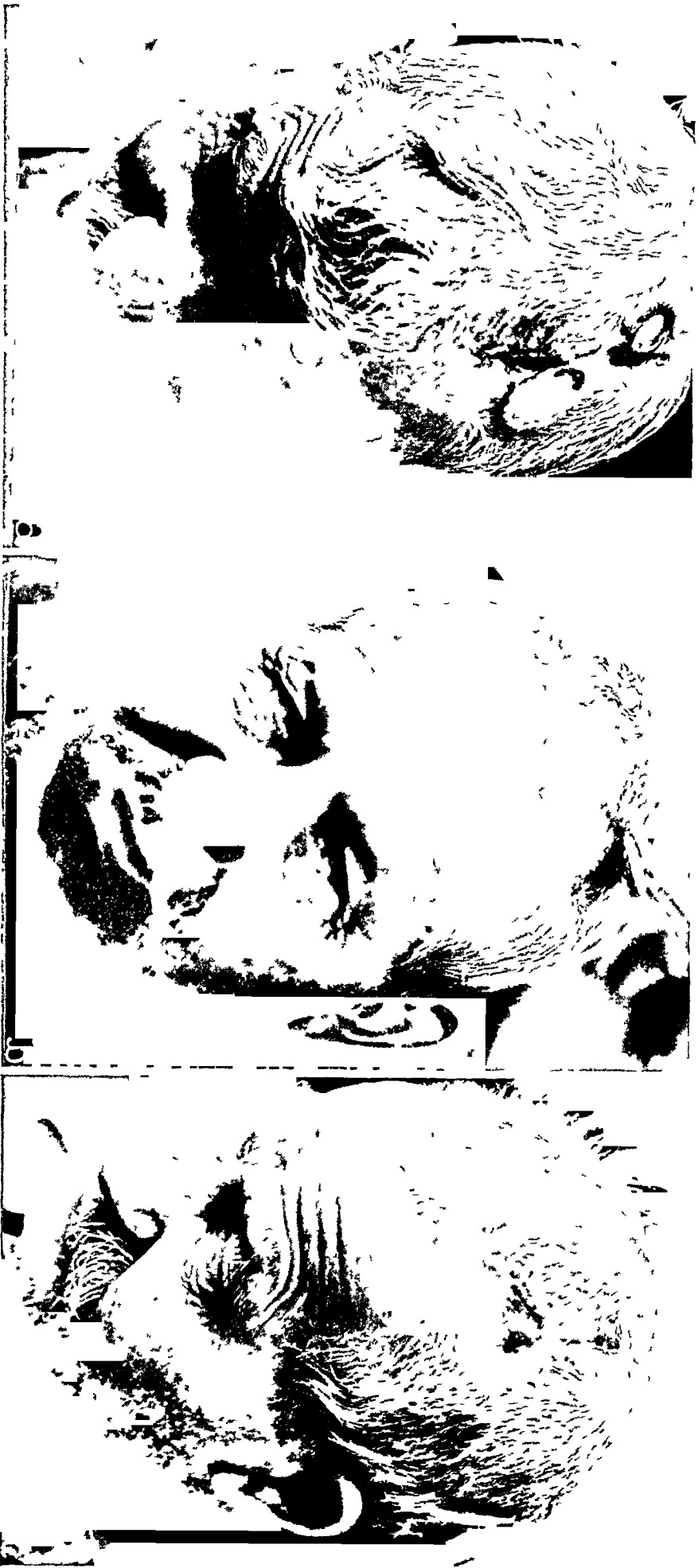


Fig 2—(A) Two electric burns on the left parietal area which had been present for five months without evidence of granulation (B) Spontaneous sequestrectomy aided by the use of a forceps, which permitted granulation and healing of the wound (C) Photograph taken six weeks following the photographs (A) and (B)

infection extending into the brain with removal of both tables of the skull, if they are necrotic, than there is when the inner table is left in place and only the outer table is removed. The dura serves as an excellent barrier to inward extension of infection provided it is not injured in the course of sequestrectomy. If extensive areas have become involved, it is reasonably safe to uncover as much as one-fourth of the skull at a time. At each stage of the operation the removal of dead and necrotic bone should be complete, however, islands of normal bone, when present, should be left in place. The periosteum likewise should be preserved and resutured after the infectious material has been removed and the field cleansed with tincture of iodine. If drainage is instituted, the drain should be removed within 48 hours, for not infrequently primary healing will be obtained. The additional areas should be treated in a similar manner at intervals of four to five days between each two operations, until all of the necrotic bone has been removed. Too often

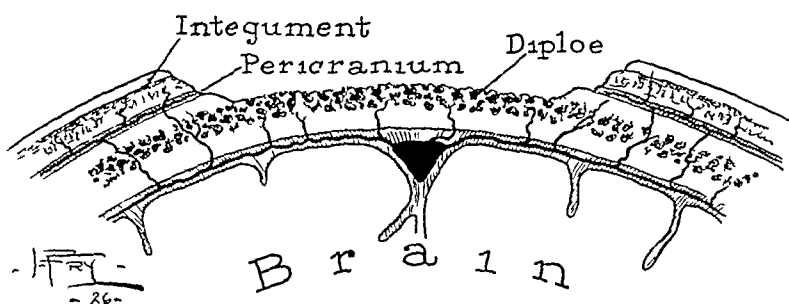


FIG 3—Drawing illustrating the importance of removing the necrotic outer table of the skull peripherally until normal bone is exposed, which also permits the edges of the skin to cover the fresh margins of the bone

the surgeon is inclined to leave dead-white bone lateral to the osteomyelitic process. If this is done, the process will continue. The dead bone should be cuetted away until bleeding appears from its cut edges (Figs 2 and 3). The bleeding can be controlled with strips of gauze soaked in tincture of iodine which, if left in place, should be removed within 48 hours, together with other drainage material such as Penrose drains and rubber tubes, *etc*

Epithelization of denuded areas of the skull can be materially hastened by removing the outer table in order to expose the diploic spaces. This will give rise to granulation tissue which serves as a bed for the epithelium (Fig 3). Skin grafts can be employed to hasten the process of epithelization. The outer table is readily removed and the first step in the removal is to make multiple openings in the outer table with the trephine bur. After this, the ridges of bone are rongueured away or removed with a chisel, care again being taken to remove all dead bone, even though it may extend under the margin of the scalp. The uncovered inner table, with its oozing diploic veins, is protected by perforated paraffin gauze, which also encourages epithelization.

Although radical surgical treatment is the effective means of controlling the osteomyelitic process, it should be borne in mind that the virulence of the organism, the resistance, and the specific immunity of the patient to the particular organism are the combative forces which determine the activity of the

process and the extent to which it will travel. This being true, active supportive measures should be employed. Administration of vaccines has been suggested and sulphanilamide has been employed, both of which have proved of value. High caloric diets with adequate vitamins are essential. Occasionally local application of heat has aided the circulation and hastened development in the zone of reaction, thus limiting the process.

The accompanying leptomeningitis is a serious complication and is controlled best by repeated or continuous spinal drainage and the administration of sulphanilamide. Again, a nourishing dietary regimen and excellent nursing are material aids in control of the disease.



FIG. 4—Roentgenogram, lateral view, showing extensive osteomyelitis of the left temporal, parietal, and frontal bones

The cerebral abscess which results from osteomyelitis is one of the suspected and serious complications. When it occurs, the surgeon is confronted with the problem of deciding whether to drain the abscess before treating the osteomyelitis or to treat the osteomyelitis before draining the abscess or, indeed, to attempt to treat both at the same time. A maxim of general surgery should be invoked in the treatment of these lesions, namely "A patient often will survive two major operations if they are performed separately but may fail to survive if both are attempted at the same time." Too much never should be attempted at one operation. Judging from my own experience, it is better to delay drainage of an abscess than to delay the operative procedure for control of the osteomyelitis. Encapsulation becomes more nearly complete if drainage is moderately delayed, whereas, the osteomyelitis process will

continue to extend and may give rise to additional brain abscesses. A number of times I have removed the necrotic bone, resutured the scalp and drained the abscess a week later through a separate incision without lighting up the osteomyelitis (Figs 4, 5, 6 and 7). There is an occasional exception, namely when the process has continued for several weeks, when the cerebral symptoms produced by the abscess are very marked, and when the osteomyelitic process is limited and apparently controlled. In those instances the cerebral abscess has been drained first and the osteomyelitis treated following removal of the drains. There is also the occasional case in which the osteomyelitic area is very circumscribed, and the abscess appears to be situated close to

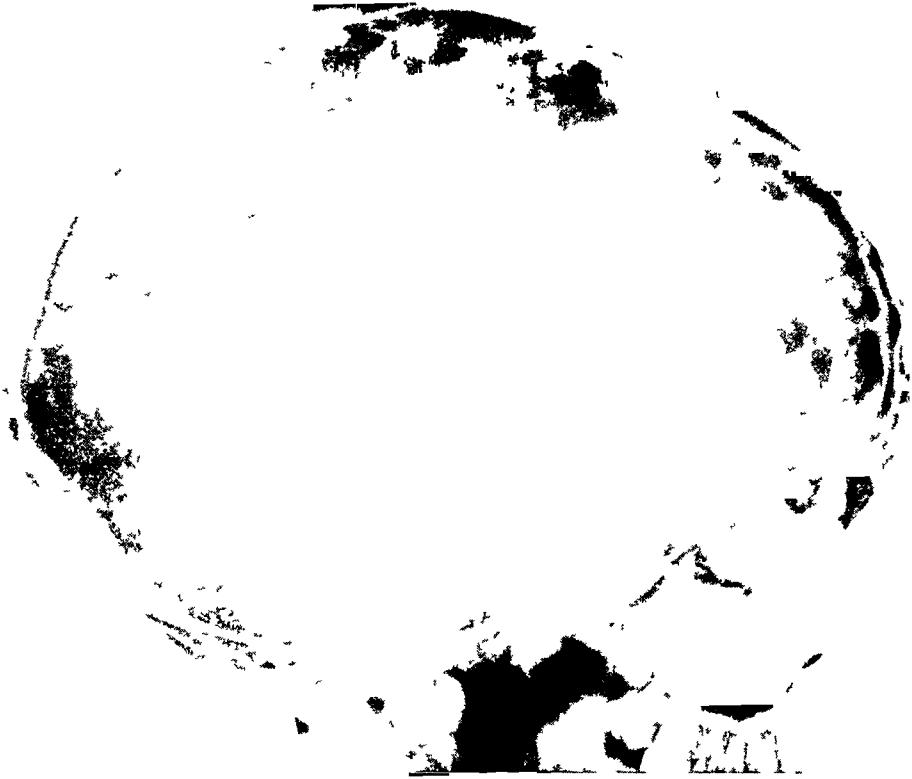


FIG 5—Roentgenogram, lateral view, made following removal of sequestrum and dead bone illustrated in Figure 4

the surface. Then it is possible to drain the abscess and remove the necrotic bone at the same time through the osteomyelitic area. There is a constant danger of producing leptomeningitis in opening the dura in the presence of infected material. There is also the danger of producing an abscess by introducing a needle through infected dura into the brain when searching for a subcutaneous abscess.

BRAIN ABSCESS—*Etiology* Brain abscess results from invasion of the brain by pyogenic organisms from acute or chronic infection of the middle ear, frontal or accessory nasal sinuses, compound fractures and penetrating injuries of the skull, infections of the scalp or osteomyelitis, and from infected emboli arising from bronchiectasis, empyema, endocarditis, and general

Fig 6—Roentgenogram, anteroposterior view, following sequestrectomy and drainage of abscess of left temporal lobe, drainage tubes in place



Fig 7—Photograph of patient following sequestrectomy and drainage of abscess of the left temporal lobe



septicopyemia^{5, 16} Although many abscesses result from an extension of the infection by contiguity, a large number develop as a result of retrograde infection of a thrombosed vein within the brain which communicates with veins that drain infected portions of the scalp, skull or meninges¹⁰ Occasionally, a stalk or channel may be found to extend from the region of suppuration to the abscess but, more often than not, the cerebral abscess is situated apart from the primary focus³² They are situated, usually, in the white matter of the brain where the veins originate and where the circulation is less abundant

Each abscess passes through three stages of development The initial stage is that of localized encephalitis which might undergo recovery spontaneously, producing a syndrome of pseudo-abscess The second stage is that of liquefaction and necrosis with encapsulation As immunity progresses, the general symptoms of infection subside The abscess becomes quiescent except for the symptoms of intracranial pressure and localization The third stage represents the terminal phase of activity Small abscesses disappear spontaneously by inspissation or resolution of the pus Large abscesses are very likely to rupture into the ventricle or subarachnoid space and produce death unless properly drained Therefore, appropriate treatment requires proper medical management during the initial stage and the selection of a suitable operation at a time when drainage will be most effective during the second stage The procedure should afford adequate drainage without spreading the infection or giving cause for recurrence of the same abscess

Macewen,³¹ in 1893, was the first to recognize and localize a brain abscess but, unfortunately, he was not permitted to operate However, he verified his diagnosis at necropsy This experience prompted him and others to advise surgical treatment for cerebral abscesses In reviewing Macewen's book, it is apparent that his good results were owing chiefly to the fact that most of the abscesses were encapsulated The encapsulation suggests that the patients were brought to him for treatment after abscesses had passed through the initial stage into the second stage of development At this time, the organisms are less virulent and many have died The immunity, likewise, has reached its maximal efficiency

Owing to Macewen's good results, many surgeons advise operation as soon as possible after a diagnosis of brain abscess has been made However, they fail to recognize the fact that clinical diagnosis has improved since his time and that diagnosis of brain abscess now is frequently made in the initial stage instead of in the second stage These early operations are responsible for the increased mortality A suppurative process of the brain is not different from a suppurative process of any other part of the body Therefore, similar reasoning and similar treatment should be employed "Wait until the abscess is ripe before opening"

Infective Agent—The organisms most frequently found in pus removed from cerebral abscesses are *Staphylococcus albus*, *Staphylococcus aureus*, pyogenic *Staphylococci*, and hemolytic *Streptococci* Other varieties of bacteria

have been found, the nature of which depends on the source and character of the cerebral contamination

Pathology—Cerebral abscesses are invariably situated below the cortex¹⁹ Occasionally, a stalk can be seen to extend from the meninges to the abscess, but more often than not, trace of path of the invasion cannot be demonstrated. The explanation for this, I believe, is that the communicating vein, which served as a path for the organism to invade the white, poorly vascularized brain tissue, has become thrombosed. The stalk, if present, represents the zone of reaction about the infected vein. Following the inoculation of the brain, a localized region of encephalitis results. This process extends by thrombosis of more capillaries and vessels until reaction and immunity limit such extension. The center of the lesion disintegrates, liquefies, and becomes pus. Proliferation in the peripheral zone results in formation of fibrous tissue and encapsulation.

I am convinced that infections may travel through thrombosed veins and diploe for long distances, to produce abscesses without osteomyelitis. This is substantiated by the fact that abscesses do result from infections of the scalp, frontal sinus, and antrum without an accompanying osteomyelitis. The reason cerebral abscesses do not always follow osteomyelitis of the flat bones of the calvarium, frontal sinusitis, disease of the middle ear, or mastoiditis, I believe, is that venous thrombosis is limited by a zone of reaction and a collateral venous circulation. Positive blood cultures are rarely obtained. Symptoms of meningitis frequently accompany cerebral abscesses.

A single embolic abscess is relatively rare. Multiple abscesses follow pulmonary disease, particularly bronchiectasis. Also, they may represent a part of a general septicopyemic infection. The virulence of organisms producing multiple abscesses is usually so overwhelming that death results before encapsulation takes place.

Penfield³⁴ stated that the wall of an abscess begins to form in the first week but it is not firm enough to offer appreciable resistance to an exploratory needle until two to three weeks have passed. The course without drainage depends on the nature and virulence of the organisms. If an insufficient wall or capsule is formed, spreading encephalitis with edema of the brain may quickly terminate the patient's life.

Extension of Infection by Contiguity—Extension of infection by contiguity is responsible for a large number of brain abscesses. The otologist often encounters an extradural abscess associated with disease of the temporal bone. Cortical abscesses of the temporal and cerebellar lobes resulting from extending infection of the ear occur but rarely. However, accompanying subcortical abscesses of both lobes are frequent, some of which have produced sufficient reaction to seal the meningeal spaces. When this occurs, it is permissible to drain the abscess at the time of mastoidectomy. If the meningeal spaces are not sealed, the introduction of a cannula from an infected mastoid wound into the brain can give rise to another abscess readily. Furunculosis of the scalp, an infected scalp wound, cellulitis, osteomyelitis, and localized

meningitis are frequent sources of cerebral abscess³⁰ Abscesses resulting from infections of sinuses are owing to inward extensions through diploic channels, emissary, dural, and cerebral veins

Relation of Frontal Sinusitis to Abscess of the Frontal Lobe—Woodward,³⁸ in considering the etiology and pathology of osteomyelitis of the frontal bone, has agreed, with others, that the *Staphylococcus pyogenes aureus* is the organism most frequently responsible for the lesion, and has stated that infection of the frontal sinus occludes the ostium and places the pus under pressure This diminishes the blood supply which, in turn, results in necrosis of the mucous membranes and thrombosis of the perforating veins From this point, the infection spreads through the diploe, preceded by thrombosis of the diploic veins whenever death of bone has occurred Pus and granulation tissue fill the diploe, which results in rapid destruction of the osseous elements Furstenberg²⁰ has regarded the frontal sinus as eroded diploe, the outer wall corresponding to the external plates and the internal wall corresponding to the internal plates of the frontal sinus, which he believes is the chief reason for extension of the infection of the frontal sinus into the diploic spaces Because the diploic veins communicate with emissary veins, it is apparent how the infection can reach the scalp or dura If the infection is overwhelming and cannot be stopped by protective reaction, it reaches the cerebral veins with a resulting cerebral inoculation Extradural abscesses over the frontal lobes are infrequent but occur often enough to warrant consideration when a diagnosis is being made Abscesses of the frontal lobe do develop from infections of the frontal sinus without accompanying osteomyelitis, just as they develop from infection of the antrum or ethmoid and from infection of the maxilla following extraction of teeth These infections undoubtedly follow perivascular spaces and thrombosed veins into the subcortical portions of the brain

Symptoms—The symptoms of cerebral abscess vary with the different stages of the disease and vary according to the systemic reaction, the degree of increased intracranial pressure, and the situation of the abscess

Patients who have a temporosphenoidal or cerebellar abscess invariably give a history of acute or chronic otitis media with a suppurating mastoid Abscesses in the frontal lobe are preceded by acute colds, frontal sinusitis, pansinusitis, and osteomyelitis of the frontal bone The sudden increase of septic symptoms following a cerebral injury suggests the possibility of a developing brain abscess Patients become apathetic and an increase in temperature occurs, the temperature remains high for the first few days but soon takes on the septic, steeple-like contour The number of leukocytes increases to 20,000 or more Examination of spinal fluid discloses an increase of pressure, increased concentration of protein, and an increase in the number of lymphocytes³⁷ If active, suppurative meningitis develops, polymorphonuclear leukocytes appear in large numbers, causing the fluid to become cloudy Also, the active organisms usually are identified

Headaches and vomiting appear early Irritability, alternating with stupor

and with rigidity of the neck muscles, is a sign of increased intracranial pressure and meningeal irritation. The pulse is full and bounding, the rate is slower than normal. Choked disks and retinal hemorrhages likewise appear when the normal flow of cerebrospinal fluid has been disturbed.²⁹

The localizing signs depend on the size and situation of the abscess. A temporosphenoidal abscess can produce homonymous defects in the visual fields, homolateral palsy of the sixth and third cranial nerves, and contralateral anesthesia, paralysis, and pathologic reflexes. An abscess in the frontal lobe may attain considerable size without producing localizing symptoms.²⁵ However, I have observed that the initial swelling about one eye is a good diagnostic sign of the lobe affected because the abscess is usually on the same side. Osteomyelitis of the frontal bone invariably extends to one side of the median line, suggesting the lobe involved. Although paralysis may not be present, contralateral reflexes may be exaggerated. When in doubt, it is justifiable to carry out ventricular studies and ventriculography. Cerebellar abscesses produce cerebellar symptoms, plus nystagmus¹¹ and reduction of homolateral reflexes. Hiccough and rigidity of the neck further indicate a lesion of the posterior fossa. Those miscellaneous abscesses that involve the brain stem and pons present bilateral pyramidal signs and bilateral palsy in the distribution of cranial nerves. Those developing from infected wounds are situated in the vicinity of the infection and those developing from nasal sinuses other than the frontal sinus are situated in the lower half of the frontal lobes.

I have seen temporosphenoidal abscesses and one cerebellar abscess produce homolateral pyramidal symptoms with partial contralateral pyramidal symptoms. The symptoms all disappeared following drainage of the abscess. The homolateral pyramidal symptoms were undoubtedly owing to partial displacement of the hemisphere by the abscess, to the opposite side, to such an extent that the crus cerebri was pressed upon and notched by the opposite margin of the tentorium at the incisura tentorii.

The pathologic process, during the initial stage of three weeks, represents a battle between destructive and reparative forces. The secondary quiescent stage, from the second to the fifth week, represents a partial victory for the forces of repair, because the abscess no longer enlarges and the pus is becoming more securely confined by a fibrous capsule. The edema disappears and circulatory disturbance, peripheral to the capsule, is repaired slowly. The recovery will continue up to five weeks, in the case of large abscesses, when apparently it comes to a standstill. During this quiescent stage the symptoms of sepsis subside and the temperature and number of leukocytes recede to normal or slightly above normal. Headaches improve, mental reactions are faster, and the number of cells in the cerebrospinal fluid returns to normal. Localizing symptoms likewise subside but, in spite of the general improvement, periodic headaches occur and choked disks and defects in the field of vision fail to disappear. Reflexes remain exaggerated and motor impairment persists. In cases of abscess of the frontal lobe symptoms of euphoria or

depression linger. The number of leukocytes continues to rise to 12,000 to 14,000. The patient, on certain days, is apathetic, refuses to eat, and prefers to lie in bed. If it were not for the history of infection and the symptoms of the initial stage, often it would be difficult to distinguish between those symptoms caused by abscess and those produced by a cerebral neoplasm.

Symptoms may continue throughout the quiescent stage for months, until the patient is operated upon, because of an erroneous diagnosis of brain tumor, or dies from rupture of the abscess into the ventricular system or subarachnoid spaces. Small abscesses heal spontaneously with disappearance of all symptoms. Symptoms of abscesses that have been drained surgically disappear, unless important tracts and cortical centers have been destroyed by the inflammatory process. Mutilating operations likewise contribute to permanent injury of cerebral tissue. Epilepsy is a sequela to localized encephalitis and abscess, and it may appear in any case in which there has been a lesion in the frontal, temporal, or parietal lobes. The incidence of this condition may be lowered by proper and adequate drainage. Subsequent resection of the scar may offer some amelioration and relief of epileptic seizures.

Surgical Considerations—It took many years to learn that performance of a hasty, emergency operation was futile and was accompanied by a high mortality.²¹ This high mortality undoubtedly will follow if the surgeon yields to insistence that he do something as soon as a diagnosis of cerebral abscess has been made.²⁴ Every cerebral abscess passes through a stage of encephalitis before encapsulation occurs. It is during this stage that the infection is virulent and is disseminated most easily. Some surgeons argue that unless the necrotic tissue is removed the patient will die. This is true in the occasional case, and cases have been reported in which aspiration of necrotic material was successful, more often than not, however, the infection is disseminated by surgical intervention and the patient dies from fulminating, suppurative meningo-encephalitis. I believe the best procedure to employ during the acute stage is supportive treatment, rest in bed, high caloric diet, spinal drainage, ice bags to the head, frequent catharsis, moderate amounts of fluids, and, if the patient is comatose, occasional intravenous administration of an hypertonic solution of glucose.

Encapsulation takes place in two to four weeks. The process is an indication that immunity is being established. It is characterized by a decrease in the number of leukocytes to 12,000 to 14,000. The temperature, likewise, returns approximately to normal, 100° F (37.8° C), or lower. The number of cells in the cerebrospinal fluid, if increased, returns to normal. The cerebral symptoms gradually subside, but seldom disappear completely until the abscess is drained. Choking of the optic disks, if present, may continue until optic atrophy results. When encapsulation and immunity have been established, thorough and continuous drainage is necessary to effect a cure without recurrence of the abscess.

Surgical Technique—The ideal exposure of a cerebral abscess is one that allows the surgeon to enter the cranium through a clean field over the ab-

cess^{2, 3, 6, 8} Exceptions to this rule are when it is desirable to avoid a scar in the frontal region or when it is necessary to pass through a zone of osteomyelitis to reach the abscess. In entering the skull through a clean field, the site is chosen where the abscess is nearest the cortex or which will give the best drainage.¹⁴ A small incision, 5 cm in length, is made in the scalp. A craniotomy 3 cm in diameter is usually large enough to afford ample exposure. The meninges and cortex are then sutured with interrupted stitches of catgut about the margins of the decompression to prevent separation of the cortex from the dura when intracranial pressure is relieved by draining the abscess. The meninges and cortex are further sealed and glued together by use of the electrocoagulating current. A crucial incision is made in the dura to expose an area of brain about 2 cm in diameter. The margins of the wound are covered with wet strips of cotton in order to minimize the spread of pus between the dura and skull. The cortex overlying the abscess is frequently edematous and cyanotic in appearance.

A round-tipped brain cannula is used to locate the abscess. The resistance of the capsule of the abscess gives one the impression that the cannula is being placed against a flexible, hollow rubber ball. If the abscess has been there for a long time, the resistance may be so great that it is impossible to penetrate the capsule without incising it. Small abscesses may be overlooked, because the firm capsule is capable of deflecting the cannula unless it is directed toward the center of the abscess. As soon as the cannula enters the abscess, the trocar is removed and a Luer syringe, with an intervening rubber connector, is attached to the cannula. The pus is gently aspirated and the cavity is cleansed with small quantities of physiologic saline solution. The cavity of the abscess is explored by incising the cortex and capsule with an electro-surgical needle, using the cannula, which has been left in place, as a guide. The capsule is opened for a distance of 2 cm in order to insert an illuminated retractor. This makes intracapsular exploration possible, permits further cleansing of the cavity of the abscess, and assures against overlooking pockets communicating with the abscess. During this procedure the capsule is retracted outward against the cortex and skull until the cavity is packed, thus preventing retraction of cerebral structures away from the skull.¹⁸

To assure against collapse of the cortex following drainage of an abscess, I fill the cavity, about the two inserted tubes, with loosely packed strips of iodoform gauze. This continues to keep the capsule moderately distended, instead of allowing it to crumple and give rise to loculated pockets within the capsule. The strips of gauze are shortened daily until they are removed on the tenth day. The gradual collapse and contraction of the capsule prevent recurrence of abscesses and the development of cerebral fungi.

The two tubes are sections of catheters. They are left undisturbed until after the gauze has been removed. One is shortened on alternating days until removed on the twenty-first day, the other is shortened as the sinus closes in and forces it out, which requires from four to six weeks. At operation, the tubes are fastened to the skin to prevent accidental removal during the daily

withdrawal of gauze Following removal of stitches, the tubes are prevented from falling out by transfixing the exposed ends with safety pins and fastening these to the skin with strips of sterilized adhesive tape Strips of vaselined gauze are placed over the margins of the wound to prevent the gauze dressings from adhering to the wound The second tubular drain occasionally is exchanged for a smaller one after the third week but at no time is the cavity irrigated, for fear of disseminating the infection The patient is allowed to get out of bed after the second day and to leave the hospital after two weeks His subsequent dressings are done at the office

Other Technics—Aspiration by needling has a limited field of usefulness¹⁷ It is most useful in draining small, sterile, deeply seated abscesses One aspiration, or two, may be sufficient to drain a sterile abscess but, when the organism still remains active, refilling continues until adequate, continuous drainage has been instituted There is also danger of spreading the infection by repeated aspiration, as it is impossible to insert and to withdraw the needle through the same tract

Treatment of the Capsule—Again I find surgeons divided in their opinions as to the best treatment of the capsule It must be accepted that if the capsule is left in place, it will result in a fibrous scar Although this does occur, can it be avoided, and should the capsule be removed at the time of the initial operation or at a later date? Macewen,³¹ Bagley,⁹ Hassin,²³ Cone¹⁴ and many others have demonstrated the pathologic changes that develop to form a capsule about the abscess From clinical experience, it is apparent that the capsule continues to thicken for several months if the abscess is unrecognized Therefore, it is fair to assume that the walls will collapse more readily and will be thinner if the abscess is drained properly as soon as immunity and encapsulation have taken place To assure collapse of the capsule, King²⁶ ²⁷ and Cahill¹² have suggested removal of the overlying cortex and the peripheral dome of the capsule King and others have suggested removal of the capsule at the initial operation This procedure hastens recovery when it is possible to remove the abscess and capsule without opening it Bagley reported such a case and I removed such an abscess but was unaware that I had done so until the mass was opened later The wound, in this case, healed per primam without any drainage My experience with removal of capsules following evacuation of the pus, however, has not been satisfactory, because secondary suppurative encephalitis develops that is more troublesome to treat than the original infection If drainage is not instituted, pus becomes inspissated and forms the caseous center of a fibrous mass The mass will contract gradually until there remains but a small nodule of what once was an abscess, 3 to 5 cm in diameter The larger abscesses are more likely to rupture into the sub-arachnoid spaces and ventricular system than the smaller ones, consequently, it is unsafe to wait for these to disappear spontaneously I cannot concur with those who believe that the rigid capsules will not collapse, for experience has demonstrated that all have collapsed, if properly drained The difficulty encountered with recurrent abscesses, attributed to failure of the capsule to collapse, I believe is owing to failure to secure adequate and continuous drain-

age Epilepsy is a symptom and a sequela that will be encountered in the treatment of suppurative diseases of the brain Medication and dietary regimens offer some assistance in the management of epilepsy If capsules or scars are to be removed, I believe it is safer to do so after the acute infections have subsided, as practiced by Penfield ³⁴

Cerebellar Abscess—Cerebellar abscesses have been the most difficult to treat of all cerebral abscesses, because collapse of the cerebellum following drainage frequently results in contamination of the subarachnoid spaces and gives rise to fatal meningitis Treatment of this group of abscesses has convinced me that the surgically sealed cerebral wound has a useful place in the treatment of brain abscesses The usual preparation and delay are employed to make sure that encapsulation has taken place It may be true that the zone of inflammation and adhesion is situated along the sigmoid sinus or petrous bone, but I have found it most advantageous to explore the cerebellum at the most accessible place, which is over the dorsum of each cerebellar lobe The technic from this point on is similar to that previously described Electrocoagulation alone cannot be relied upon to seal the meninges and the cortex but must be combined with the use of numerous interrupted stitches of fine catgut to transfix the meninges and cortex around the margins of the limited cerebellar exploration Leakage of cerebrospinal fluid must not occur The brain cannula should be directed in an outward, upward direction to avoid entering the fourth ventricle Otherwise the standard technic is used

SUMMARY AND CONCLUSIONS

The surgeon should employ supportive measures, such as high caloric diets, also, when the infection is the result of Staphylococci or Streptococci invasion, occasional administration of vaccine and sulphanilamide are helpful

Osteomyelitis of the skull should be treated similarly to osteomyelitis of other bones, this treatment consists of thorough sequestrectomy and removal of all dead bone The wound should be cleansed with tincture of iodine and, if drainage is instituted, the drain should be removed within 48 hours and the scalp closed with sutures of silkworm gut

Mortality will be lowered in the treatment of cerebral abscess if the surgeon employs some of the same principles that are employed in the treatment of suppurative lesions elsewhere in the body ²¹

In cases of suspected cerebral abscess resulting from infections about the ear, with indefinite localizing symptoms, or with localizing symptoms and signs that are conflicting, I have observed the rule of exploring the temporosphenoidal lobe before exploring the cerebellum on the side of the infected ear because of the higher ratio of incidence of temporosphenoidal abscess

If, on study of the physical and neurologic signs, I fail to localize a suspected abscess, performance of cerebral pneumography is justifiable

Adequate and continuous drainage should be instituted after encapsulation has taken place

If capsules are to be removed, it is better to remove them after the acute infection has subsided

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DISCUSSION—DR FRANCIS C GRANT (Philadelphia, Pa) Doctor Adson has called attention to two very important points in the treatment of osteomyelitis First, the retention of the pericranium, because from that pericranium, new bone will regenerate I should like to detail a case which will substantiate Doctor Adson's opinion I should also like to ask Doctor Adson about his treatment of the more acute osteomyelitic cases We see, through the nose and throat service, a good many cases of acute frontal sinusitis which develop into acute osteomyelitis of the frontal bone and spread rapidly through the bone That is the type of case of osteomyelitis which certainly, in our opinion, is very much more difficult to handle than are the chronic cases

A female, age 12, was admitted to the hospital in 1934, following bilateral frontal sinusitis resulting from diving She developed an acute osteomyelitis which involved both frontal bones We had to take off all of her frontal and temporal bones on either side This was accomplished in two stages, necessarily so, because her condition was poor, but we finally were able to get beyond the edge of the infected bone These operations were performed in January and February of 1934 After a prolonged convalescence the wounds healed Skin grafting was necessary

Roentgenologic studies, in May, 1934, showed that nearly all of both frontal bones and over half of each temporal bone had been removed But the pericranium had been preserved Subsequent roentgenograms, in October, 1936, showed practically complete regeneration of the débrided bone (Case of Gunshot Wound of Head and Case of Osteomyelitis of Skull ANNALS OF SURGERY, 102, 473-475, September, 1935)

I should like to ask Doctor Adson one question concerning the treatment of subcortical abscess in the brain. Does he believe in cortical incision with subsequent insertion of packing into the abscess cavity or in simple tap and insertion of tube drainage?

We reviewed 31 cases that were available in the Neurosurgical Clinic, from the standpoint of morbidity, to see which group of patients had the most satisfactory final result.

We believe that the smaller the opening in the cortex to tap, or tap and drain the abscess, the more satisfactory results you will obtain, when these patients are reviewed a year or two later. We found that of 23 cases treated by tap or tap and drain, but five had hemiparesis, convulsions or other symptoms of a serious nature. In eight cases, in which a cortical incision had been made to introduce drainage, seven had a hemiparesis or a history of convulsive attacks.

I am not referring to the immediate mortality but entirely to the morbidity, and my impression is, in the treatment of abscess, if you can handle the case successfully by tap or tapping and tube drainage, the eventual results seem to be very much better.

DR GILBERT HORRAX (Boston, Mass.) There is just one aspect of Doctor Adson's paper on which I would like to comment, and that is the treatment of the brain abscess. I feel as he does, that we have three available methods, the first of these being the simple one, which Doctor Grant has mentioned, of tapping the abscess and seeing if it is a type with which you can deal in that way. If the abscess is sterile, or in some instances if it is not sterile and can be frequently tapped, this will be sufficient, and I think undoubtedly the sequelae are less.

On the other hand, it has been my experience, as it has that of others, that there are many abscesses in which tapping is not curative. They show signs of increased brain pressure again very soon in spite of frequent tapings, and one must do something more radical for them.

In our series of 18 chronic abscesses, there were three that were handled successfully by tapping. Many of the others were tapped several times and then we had to do something more serious and more radical with them.

The second method is the open method of drainage which, as Doctor Adson says, was founded by Macewan, and if one goes back to his treatise, as we all do who are dealing with this sort of thing, one will find that his great success was not only the fact that the abscesses were long-standing and well encapsulated, but that he did use this wide open drainage, that is, a relatively wide opening, which Doctor King subsequently adopted in this country in a modified form, and with which he has been so successful.

I think the principle is the same, whether one uses Adson's, King's or Doctor Cushing's method, which consists of marsupialization of the abscess. The latter I have found more successful because many of these abscesses are near enough to the surface and the capsule is of such great strength that you can take sutures through it and sew it to the galea, and thus make a pouch of the cavity and have it entirely extracranial.

I have not seen any cases in which it was necessary to seal off the meninges. I have never seen a case where infection took place by meningitis in that way. It is always by an extension of an osteomyelitic process or by rupture into the ventricle. If the abscess is near enough to the surface, the thing to do, as Doctor King does, is to uncap that area, get down to the abscess and empty a part of its contents. The capsule will then protrude toward the surface, so that one can put in sutures and sew these to the galea, and have a perfectly outside tube, so to speak.

The third method is the one which Clovis Vincent has been advocating so much recently, of extirpating the abscess. We all run into these occasionally and I think that is a method which is very good at times, if the abscess is so situated that one can do it safely, but I do think if one can make use of the simpler methods, the sequelae are going to be less.

DR JAMES MONROE MASON (Birmingham, Ala.) I was much interested in the remarks concerning osteomyelitis following denudations of large areas of the skull. Some years ago, it fell to my lot to care for two men who, within a few days of each other, received electric burns involving, in one instance, a large area of the scalp over the left parietal bone, and in the other, large areas over the frontal and occipital bones.

The progressive development of the osteomyelitis in the three bones followed along lines which so closely paralleled each other that it suggests what may be expected to take place whenever large areas of the bones of the vault of the skull are denuded of their coverings.

In the burns involving the frontal and occipital bones, the soft parts soon sloughed off and were trimmed away and the underlying bone was dressed antiseptically until such time as the sequester should become loosened. This took place within a few weeks, and the loosened bone was lifted off. We found, in each instance, that the entire outer table had become detached, but that the inner table was viable and remained in place except for a small area near the center of the wound. The entire thickness of bone was necrotic and came away with the detached outer table, leaving the dura exposed at this point. The wounds were covered with grafts and the patient recovered.

In the case involving the parietal bone, the same plan of treatment was employed, but the outcome was not so fortunate. About three weeks after the receipt of the injury, the patient suddenly developed hemiplegia and died very shortly from a large brain abscess. Autopsy revealed a similar condition in the progress of the osteomyelitis which we had observed in the other case, namely, that the entire outer table was becoming necrotic, that the greater part of the inner table was resisting the process, but that a point at the center of the involved area of bone was also necrotic. The progress of the infection went entirely through the bone at this point and a small subdural abscess had developed. This quickly extended to the brain and a large abscess was found in the parietal lobe.

Apparently, in large flat bones of the skull the inner table receives sufficient nutrition from vessels surrounding the involved area to insure its vitality when the outer table is denuded, but the circulation near the central part of the inner table may not be sufficiently active for its preservation, and necrosis follows, allowing infection to come directly in contact with the dura.

It is suggested that in large denudations, sections of bone corresponding to the center of the area be removed at once, in order that the tendency to necrosis of the inner table at this point be checked and the danger of the development of brain abscess be lessened.

DR ALFRED W. ADSON (closing) In reply to Doctor Grant's question, may I state that when the osteomyelitis is limited to the tables of the frontal sinus the lesion is treated by the otolaryngologist. If the lesion extends to the tables of the frontal bone, the operation is divided into two portions. The disease of the frontal sinus is taken care of by the otolaryngologist and the disease of the frontal bone, by the neurosurgeon.

I prefer to seal the meninges to the brain, as described, rather than to employ the technic of extirpation of the abscess, since thus there is less danger of contaminating the subarachnoid spaces. This is especially true of cerebellar abscesses.

RAPID CONTROL OF INTRACRANIAL PRESSURE

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THE present methods for the control of increased intracranial pressure require some time to become effective and depend upon certain physiologic principles. Even if these principles may be questioned on experimental and clinical grounds,^{1, 2, 3, 4, 5, 6} from clinical evidence the mortality rate has declined under this method of treatment. Munio,⁷ in 1925, reported a series of cases collected from the literature with a mortality rate of 37.8 per cent.

Fay⁸ reported a series of cases in which those patients who survived six hours after admission showed a 10.4 per cent mortality, and Ochsner⁹ reports a total mortality rate of 8.4 per cent. By excluding those patients who died in the first 24 hours, a mortality rate of 3.9 per cent was obtained. The method for controlling intracranial pressure we wish to present depends on mechanics alone, is rapid, and we think effective in most cases. Within the cranial cavity there are three substances that are important. Munio¹⁰ pointed this out in 1783, and Kellie,¹¹ in 1824, elaborated the idea. These are the brain substance, the blood vessels with their contained blood, and the cerebrospinal fluid. A change in the volume of one means a change must occur in the volume of one or both of the other substances. The result is that the pressure in the blood vessels, especially the veins, as was pointed out by Grinker,¹² is increased and this pressure causes a rise in the systolic pressure with a slow, full pulse, with an increased pulse pressure, in the systemic circulation. Cushing called attention to the fact that our museums have many examples of fractured skulls, but there were very few examples of injured brains, and that after all the brain itself was more important than the fracture. While our clinical evidence indicates that the mortality rate is improved, little or no attention is paid to the morbidity resulting from cranial injuries.

Lowenberg, Waggoner, and Zbinden,¹³ Caine,¹⁴ Davies,¹⁵ Hahn,¹⁶ and McKean Downs¹⁷ have called attention to the effect of anoxia on the brain in nitrous oxide anesthesia. Lowenberg, Waggoner, and Zbinden report three cases in which there was destruction of the cortex and basal ganglia following the use of nitrous oxide oxygen anesthesia, and one case with clinical evidence of a similar process. These authors point out that death occurs at varying times following the start of the anesthesia, varying from 20 seconds to an hour and a quarter, or it may be hours, days, or weeks before death takes place, or the case may recover with residuals present after years. Signs of anoxemia do not necessarily have to be present. Lowenberg, Waggoner, and Zbinden consider two possibilities: (1) Asphyxia, and (2) toxic effect of the gas. They find support for both ideas, but believe that the toxic effect of the gas is the more likely cause of the destruction.

Couville¹⁸ reports 13 cases, nine of which died. He considers that anoxemia is one of the factors causing changes in the brain and develops a pathology which shows (a) A sclerosis of scattered pyramidal cells, (b) discrete pale areas in the cortex, (c) patchy necrosis of the superficial, intermediate, deep, or all cortical layers, (d) a subtotal destruction of the cortex, or, (e) if the patient survives for a sufficient interval, a vascular scar may result due to the formation of new blood vessels. Cellular changes are noted in the individual cells. Anoxia has been given little attention. All tissues of the body may be injured, and the degree of anoxia and the length of time necessary to effect damage vary with the individual case. The anesthetist by producing anoxia during the anesthesia can produce symptoms comparable to those resulting from cerebral trauma, and from Caine's case one can see how permanent the damage can be.

The physiologists recognize a critical blood pressure of 80 Mm. of mercury. Clinically, if the systolic pressure remains at this level for 30 minutes or longer, with a very rapid pulse, the patient may be in serious danger. If the pulse is slow, there is no danger. With the development of increased pressure in the cranial vault, the supply of oxygen will vary. The patient may recover, but have irreparable damage of the brain tissue, giving a morbidity which is almost entirely overlooked. The results of the present methods of reducing intracranial pressure require several hours, and extensive damage may take place. There are other times when a quicker relief of intracranial pressure is desirable. This mechanical method was called to our attention, in 1931, by J. R. Learmonth in a case where the increased intracranial pressure was causing vomiting and headache, in a young girl upon whom Learmonth had operated, and found a medulloblastoma. Following the suboccipital decompression and subsequent deep therapy, there was improvement for a time. With the return of pressure, life became unbearable for the patient. A ureteral catheter, No. 6 Fr., was inserted into the ventricle through the old trephine opening, the pressure released, and as long as the drainage was effective, the patient was comfortable.

Fay and Chamberlain¹⁹ have called attention to the fact that if the cerebrospinal fluid can be reduced 1 cc. in volume and kept that way for an hour, it would mean 120 cc. of extra blood to the brain. Ten cubic centimeters' reduction for one hour would mean 1,200 cc. This brings up a number of possibilities when the various problems of increased intracranial pressure are considered, for by means of continuous ventricular drainage, the cerebrospinal fluid volume may be reduced rapidly and for longer periods of time.

The method consists of inserting a No. 6 Fr. ureteral catheter through a trephine opening in the skull. The ventricle is first punctured with an ordinary ventricular puncture needle in order to make a path. Into the ureteral catheter the stylet of the ventricular needle is placed, so as to make it firm. The stylet and catheter are introduced into the ventricle through the previously formed path made by the ventricular puncture. The catheter is anchored with a very fine linen stitch to the skin. The top of the catheter

should be a little above the skin to prevent the skin from closing over the catheter. A 1-2,000 biniodide of mercury dressing is placed over the catheter end. The catheter may become occluded. It is opened by inserting into the catheter a long needle, and then aspirated. After a week or more, suppuration may develop at the skin, and the catheter has to be removed and inserted on the other side. However, the catheter may be kept for longer periods, depending upon the development of suppuration at the skin. We have used this method in 24 cases for the following reasons:

Preoperative reduction of cranial pressure to help stabilize the patient and to prevent sudden pressure changes at the time of operation. Case 14 illustrates this point.

Case Report—J. W. C. (Hosp. No. 97921), male, age 4, had a posterior fossa lesion. A suboccipital exploration, under novocaine block, was attempted. With the completion of the injection, the patient stopped breathing. When turned on his back, breathing promptly began. Thirteen days later, a general anesthesia was attempted, with the same result. Four days later the patient was placed on his side and a ventricular drain inserted. The cerebrospinal fluid was under great tension. In three days the drainage was less profuse, and ten days later a general anesthesia, intratracheal, was given and a suboccipital exploration revealed a spongioblastoma extending from between the cerebellar hemispheres into the fourth ventricle. He died that night with hyperthermia and signs of medullary failure.

Because of the increased intracranial pressure this patient could not be placed face down. By relieving the pressure, the operation could be postponed, and he could rehabilitate himself. We have used ventricular drainage in patients with high intracranial pressure to give them a period before operation to allow them to habituate themselves, and to obviate the sudden release of intracranial pressure at the time of operation.

Postoperatively we have used ventricular drainage to prevent pressure developing, and making for a smoother convalescence. Fluids are not kept at low levels, and the patient does not need to have repeated injections of hypertonic sucrose or magnesium sulphate enemas.

When operation has failed to remove the cause of the intracranial pressure, ventricular drainage contributes to a smoother convalescence and puts the patient in better condition for radiation therapy.

By relieving the increased intracranial pressure, symptoms and physical signs may develop that will aid in diagnosis, or signs that are due only to increased pressure may disappear.

Horrax suggested that when ventriculography was undertaken, in order to prevent the development of an acute increase in the intracranial pressure, the patient should be operated upon the same day. If symptoms of pressure arise following ventriculography, a catheter inserted into the ventricle will reduce the pressure and there is no need to perform an emergency operation.

Cerebral hernia with separation of wound edges resulting in cerebral fungi may be controlled and the skin edges will heal. Case 2 had to have the bone flap removed because, in spite of all attempts at reducing the pressure, the

duia could not be closed. The skin was closed, but in several days there was a gaping of the wound with some visible brain substance. Various attempts to get the wound to heal were of no avail. A ventricular drain was then inserted, and in four weeks the skin had completely healed. By a judicious use of ventricular drainage, postoperative hernia may be avoided.

We have not used ventricular drainage in cranial injuries. The other conservative measures have been sufficient, but we would not hesitate to use it when conservative measures failed.

Of the questions that arise as to the complications consequent to employing this procedure, naturally the first is infection. It is a definite risk. Of the 24 cases, six showed definite cloudy fluid. A careful examination of the protocols will show that this is not associated with the length of time the drains were left in. It also shows that a cloudy fluid will clear up (Cases 1 and 15). In the 24 cases, nine are alive and 15 died. Of the six cases with cloudy fluid, their periods of drainage varied from five to 60 days. Two of these cases recovered, one (Case 1) was drained 32 days, and another (Case 15) was drained 39 days. The other cases, 18 in number, were drained from eight hours to 79 days (Table I).

TABLE I

INCIDENCE OF DEVELOPMENT OF INFECTION AFTER DRAINAGE

Case	Infection	Drainage Time	Result
1	Positive—Cloudy fluid 7 days	32 days	Recovered
2	Negative	40 days	Recovered
3	Negative—(New catheter 8 days P O)	13 days	Recovered
4	Negative	10 days	Died
5	Negative (Patient expired same evening. Temperature 106° F. Intracranial pressure not increased)	8 hours	Died
6	Negative	28 days	Recovered
7	Negative	8 days	Recovered
8	Positive (16 days after insertion developed parotitis. Culture showed strep, staph, and encapsulated gram-negative bacilli (<i>Klebsiella ozaenae</i>))	17 days	Died
9	Negative—Catheter lost	79 days	Died
10	Negative	21 days	Died
11	Negative	11 days	Died
12	Positive—22 days	60 days	Died
13	Negative	9 days	Died
14	Negative	10 days	Died
15	Positive—15 days	39 days	Recovered
16	Negative	12 days	Recovered
17	Positive—10 days	18 days	Died
18	Negative	14 days	Died
19	Negative	3 days	Died
20	Negative	6 days	Died
21	Negative	10 days	Recovered
22	Positive—6 days	7 days	Died
23	Negative	25 days	Died
24	Negative	22 days	Recovered

There were postmortem examinations in 13 of the 15 deaths. Nine cases showed no evidence of infection, four cases showed definite evidence of infection. Of the four cases with positive fluid findings antemortem, two showed definite evidence of infection, in one case there was no postmortem. Case 12 showed a purulent sphenoiditis with erosion of the sella turcica, brain abscess, and purulent ependymitis, but the pathologists believed this to be secondary to a suppurating sphenoiditis with erosion of the sella turcica (Patient had an angioma removed at operation). Case 8 showed nothing. Case 22 showed an empyema of the lateral ventricles, the third ventricle, and a basilar meningitis.

TABLE II

TIME OF DRAINAGE IN POSITIVE CULTURES OF SPINAL FLUID

Case	Development of Infection after Drainage	Result
1	32 days	Recovered
8	17 days	Died
12	60 days	Died
15	39 days	Recovered
17	18 days	Died
22	5 days	Died

Eighteen other cases drained from 8 hours to 79 days. Of 24 cases, 9 recovered and 15 died.

TABLE III

POSTMORTEM EVIDENCE OF INFECTION

Case	Evidence of Infection
4	Negative
5	Negative
8 (Positive culture)	Negative
9	Negative
10	Local meningitis Fluid clear
11	Negative
12 (Positive culture)	Infection started in purulent sphenoiditis Purulent ependymitis
13	Negative
14	Negative
17 (Positive culture)	No postmortem
18	Showed sporotrichosis
19	Negative
20	Negative
22 (Positive culture)	Positive
23	No postmortem

When we analyze the four cases with positive postmortem findings (Cases 8, 12, 17 and 22), we find Case 8 developed a parotitis that responded to treatment, and, because of high pressure, the drainage was continued. There

was an exudate over pons, medulla, inferior portion of the cerebellum, and onto the occipital lobes extending forward to the optic chiasma. Case 12 developed secondary to a suppurative sphenoiditis with erosion of the bone, brain abscesses and purulent ependymitis with purulent bronchitis and bronchopneumonia. Case 17 showed scattered granulomatous lesions secondary to a sporotrichosis, and Case 22 showed an empyema of the lateral ventricles, third ventricle, and a basilar meningitis. Case 18, with a parotitis, Case 12, with a suppurating sphenoiditis with extension, and Case 17, secondary to a sporotrichosis, can hardly be attributed to ventricular drainage. Case 22 is directly attributable to ventricular drainage (Tables III and IV). The first

TABLE IV

SUMMARY OF SIX CASES WITH
POSITIVE CULTURES

Two Recovered—Cases 1 and 15
Four Died—Cases 8, 12, 17 and 22

- Case 8
 - Drained 17 days
 - Infection developed after drainage 16 days
 - Parotitis developed 4 days after ventriculography
- Case 12
 - Drained 60 days
 - Cloudy fluid after drainage 22 days
 - Bronchopneumonia after drainage 24 days
 - Had a purulent sphenoidal sinus with erosion of bone and extension to cranial cavity
- Case 17
 - Drained 18 days
 - Ten days after drainage, cloudy fluid. At same time developed pulmonary congestion, bronchopneumonia and urinary infection
 - No postmortem
- Case 22
 - Drained 7 days
 - Cloudy fluid developed after 6 days
 - Empyema of lateral and third ventricles
 - Basilar meningitis

drain ceased to function, and a new drain was inserted through the old pathway. The symptoms of infection and cloudy fluid developed soon afterward. Of the 15 deaths, the 13 postmortems showed no evidence in nine cases. Of the four cases that showed postmortem evidence, only one case can be attributed to the method (Table V).

Repeated roentgenologic examinations of patients with ventricular drains in place have been made, and very little or no air has been found in the ventricles. While attention has been called to the irritating effect of air in the ventricles, we were unable to prove that it played any rôle in ventricular drainage.

Drainage of the ventricles was not possible unless there was increased pres-

sure present The catheter would become occluded very quickly, which we believe enhances very greatly the entrance of infection into the ventricle

The infection around the catheter at the skin edge varies a great deal The length of time the catheter is present has no relation to it Catheters have been present for many days without any infection developing In some cases, infection is present as soon as it can develop We believe the presence or absence of infection depends on dosage, virulence of the bacteria, and the local and general resistance of the patient

TABLE V
SUMMARY OF POSTMORTEM EVIDENCE
OF INFECTIONS

9 Cases—No postmortem evidence
2 Cases—No postmortem obtained
4 Cases—Positive evidence of infection
4 Cases—Positive cultures
2—Positive postmortem findings
1—No postmortem
1—No findings

In the 24 cases, we lost the catheter in Case 9, due to its slipping into the ventricle, and, at postmortem, it was found to have migrated into the anterior part of the ventricle and imbedded itself for a distance of about 1 cm into the cerebral tissue This case was drained 79 days, and the ependyma showed no evidence of inflammation

Catheters have been fixed by using a fine cambic needle with a linen thread, the suture going through both the catheter and the skin, it is then tied This has proved to be most satisfactory

SUMMARY AND CONCLUSIONS

While physiologic methods are available to control intracranial pressure, we present a mechanical method that is not new, for it has been employed in meningitis, to relieve pressure in hydrocephalus, and in reducing pressure preparatory to deep radiation It is rapid, and in case of the cerebrospinal fluid will reduce the volume as long as the drain works We have used it in 24 cases and found it to be of aid in reducing increased intracranial pressure preoperatively and postoperatively, to stabilize patients who have had pressure for some time, to aid in diagnosis, to reduce emergency operations after ventriculograms or in acute or high intracranial pressure, and to heal the skin over cerebral hernia There is a real danger of introducing infection, and, because of this, we feel that this procedure is one that must be used carefully and only after weighing the indications Cushing's use of ventricular puncture in cases of increased intracranial pressure at the time of operation greatly widened the operative field in neurosurgery This procedure may aid in its application to a still wider field

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DISCUSSION —DR ALFRED W ADSON (Rochester, Minn) I wish to support what Doctor Schmidt has said We have had occasion to use continuous ventricular drainage in a number of instances Occasionally ventricular drainage is performed in connection with a ventriculogram and then it is found that it is impossible to continue with the craniotomy the same day, which I prefer to do whenever possible In that event, we have introduced a catheter into the ventricle to control intracranial pressure until the next day This is of special value when there is present an extensive hyperencephalitis owing to a block in the aqueduct or in the region of the fourth ventricle

At one time we used a ureteral catheter, but during the last few years we have been using a No 10 French urethral catheter, which is larger and is less likely to become plugged Thus we diminish the danger of ependymitis by adjusting the catheter We also have employed it when we have been

called upon to drain a ventricle following craniotomy in cases in which repeated ventricular taps are necessary

In a number of instances, we have been compelled to resort to continuous ventricular drainage when it was impossible to remove the lesion. On a few occasions we have been able to withdraw the catheter when the block was relieved by irradiation of the tumor.

We have had cases in which ependymitis has developed. I think it has occurred less frequently when the larger catheter has been used. We have also had the catheter slip into the ventricle.

DR. HOWARD LILIENTHAL (New York, N. Y.) I would like to suggest that instead of using a ureteral catheter, which seems to me to be rather a rough sort of thing to use in the brain, a very thin, pure silver catheter be employed, or, if there are objections to that, have a thick-walled cellophane catheter made, which is absolutely nonirritating. It seems to me that these would be preferable to the ureteral catheter, which cannot really be sterilized.

PROGRESSIVE EXOPHTHALMOS ASSOCIATED WITH DISORDERS OF THE THYROID GLAND

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PRIOR to 1931, a review of the literature showed no concurrence of opinion as to the reasons for the progressive exophthalmos occasionally seen following thyroidectomy. At that time our experience with a severe case resulted in the proposal of an operative treatment which was successful and which permitted an investigation of the pathologic changes involved^{1, 2}. Since then, additional experience has been gained from the observation and treatment of a considerable number of cases, so that now, the pathologic changes involved in this condition have been verified repeatedly by numerous observers, and the value of properly directed surgical treatment is well supported. The interest of many workers relative to the etiologic factors involved has also thrown light on the cause of this serious condition. Our consideration has been given to one particular group, namely, those patients who have progressive exophthalmos associated with disorders of the thyroid gland, and in whom the exophthalmos has progressed to the point at which both the patient's vision and his life are threatened. In the past, in this severely affected—but fortunately small—number, protrusion of the eyes progressed until ophthalmitis resulted, and death invariably occurred from orbital infection and resultant meningitis. Varying degrees and rates of progression of exophthalmos are commonly seen and, in the majority of patients, the proptosis, fortunately, becomes arrested before it reaches an extreme stage.

Many questions remain unanswered concerning the exophthalmos of thyroid disease. For a number of reasons, it has been impossible to secure all the exact information that one might like in order to form an opinion on the relation of exophthalmos to thyroid disease. Clinical records indicate that 50 per cent, more or less, of patients who have exophthalmic goiter present exophthalmos. These figures actually mean little or nothing for the following reasons. A clinical notation of the presence of exophthalmos is ordinarily made when the patient has eyes which appear prominent, with wide lid slits, and a staring expression. By definition, exophthalmos is an abnormal protrusion of the eyeball, but the opinion of even a skilled clinical observer is valueless as to this point except in the most advanced cases, and even then the most experienced are unable to approximate the actual exophthalmos as shown by measurement. In addition, the relation of the eyeball to the orbit shows very wide normal variations. Without knowing the exophthalmometer reading prior to the onset of the disease, one may be unable, even after measurement, to express an opinion as to whether or not there has been abnormal protrusion. Alterations in the position of the eyeball, however, can be fol-

lowed so that progressive changes in its position can be accurately measured and judged. Our own hospital records and the writings of various clinicians expressing opinions as to the presence or absence of exophthalmos in a given series of cases are inaccurate and all but valueless.

Clinical impressions based upon the appearance of the patient are almost entirely dependent upon the width of the lid slits, and changes of several millimeters in the position of the eye with reference to the orbit cannot be appreciated. Even with extreme degrees of exophthalmos, if the lid slits are narrow, a very erroneous impression is gained, and even marked degrees of exophthalmos may not be appreciated at all. Granting that our use of the term exophthalmos is loose and inaccurate, one cannot say much more than that, after an operation for goiter, the apparent exophthalmos disappears in about one-half of the cases and lessens in an additional 15 or 20 per cent. In others it may remain unchanged, but in a few there will be progression of varying grades. This progression may continue slowly, causing no more difficulty than that involved in an unsightly appearance of the patient, progression may halt at any time and it is, fortunately, in only a very small number that it will progress to the danger point.

Previous publications^{1 2 3 4} have referred to and reviewed the varied and ineffective methods of treatment that had been tried, such as sutures of the lids, tarsorrhaphy and canthotomy, various plastic operations on the conjunctiva, incisions of the lids or removal of fat, the Kionlein operation, and section or removal of sympathetic nerves. In connection with the latter, it has been demonstrated that the width of the lid slit is lessened and the appearance of the patient altered by such operations on the sympathetics, but no change occurs in the relation of the globe to the orbit. In a group of patients in whom improvement of the appearance is the aim, a similar result can be achieved by advancing the outer canthus by a suture which will narrow the lid slit. While in animals, stimulation of the sympathetics can produce protrusion of the eyeball through stimulation of the smooth muscle fibers of the orbit, actual protrusion by this means does not occur in man. Sympathetic effects are indicated in human beings only by widening of the lid slits, alteration of the pupil, and vasomotor changes, without alteration of the position of the globe.

From personal communications and reports in the literature, operations for this condition have been performed by Doctors Semmes, Crutchfield, Horrax, Adson, Craig, McKenzie, Teachnot, Oldberg, Ochsner, Dandy, Mixer and White. The cases of these surgeons, with our own eight, make a total of 31. In this series, two deaths were reported and four results were considered poor. One of the poor results was in our own series, operation did not halt the condition, so that later the enucleation of one eye was necessary and the cornea was badly infiltrated in the other. In the patients reported by other surgeons as having poor or unsatisfactory results, it is notable that no eyes were sacrificed and there were no late deaths from meningitis caused by progression of the condition. Considering the hopelessness of these severe

cases of progressive exophthalmos when untreated, the results have been astonishingly gratifying

In our eight patients who suffered from severe progressive exophthalmos requiring operation, the age varied from 28 to 53 years. Four were females and four, males. All had marked thyrotoxicosis at some time. All had had thyroidectomy for the characteristic symptoms of toxic goiter. These symptoms were relieved by operation but there was no effect on the exophthalmos. Usually, in two months or thereabouts, some progression of the exophthalmos became evident. At the time they presented themselves for treatment, their basal metabolic rates varied from normal to minus 32. Progressive protrusion of the eyes was associated with puffiness of the lids, particularly the upper lids, usually with a large finger-like fold toward the inner canthus. Later, edema of the conjunctiva and limitation of movements of the eyes appeared. About one-half of the patients had varying degrees of choked disk, with hemorrhages. Depending upon the stage of the process, there was a protrusion of mucous membrane from beneath the lower lids. In more advanced stages, corneal ulceration had begun. Vision varied, depending on the condition of the cornea and the stage of involvement of the optic nerve. The highest degree of choked disk was four diopters. In one or two instances altitudinal hemianopsia was present. Before operation, exophthalmometer readings varied from 26 to 34. The lacrimal glands were frequently palpable. Some aching and discomfort referred to the orbit was usually present, increased by efforts to look to the side. All of the patients showed some limitation of movements of the eye muscles, the upward movement of the globes usually showing the most impairment, in only one instance were the downward movements more limited than the upward. Lateral movements were usually greatly affected, frequently reduced about 50 per cent, in others, only faint lateral movement of the globe was possible. Retrobulbar resistance was always greatly increased and readily appreciated. Intra-ocular tension was not altered. Frequently, by raising the lids, the insertions of the recti muscles could be brought into view. In the cases of most marked protrusion, the upper lids could be slipped entirely behind the globe.

Immediately following surgical treatment, there is very marked recession of the eyes. Later, in convalescence, edema of the orbital content appears, causing the eyes again to protrude to about their original position, and there may be an increase in chemosis or protrusion of the mucosa if this was present before operation.

The pathologic changes responsible for progressive exophthalmos of this type seem to be constant. In all of our eight patients, the orbit was tightly packed with the swollen extra-ocular muscles (Fig. 1). These varied in size, being estimated at from five to ten times normal in volume, their color and size depended upon the stage of the pathologic process, often they were pale. The degree of fibrosis varied considerably and the texture of the muscles varied with it. In most cases the muscles were large, slightly paler than normal, firm, and somewhat rubbery. On removing small snips for pathologic

examination, the fibrosis may be readily appreciated and actual hyaline change may be present. In our own eight patients, various minute pieces of tissue were taken from both orbits and from the various muscles, and some 25 fragments were examined. In addition, microscopic examination was made of muscles in 21 patients operated upon by others, and the same pathologic condition was found. In this clinic, Dr Charles Connor, Professor of Pathology, reported as follows: "The ocular muscles show varying degrees of degenera-

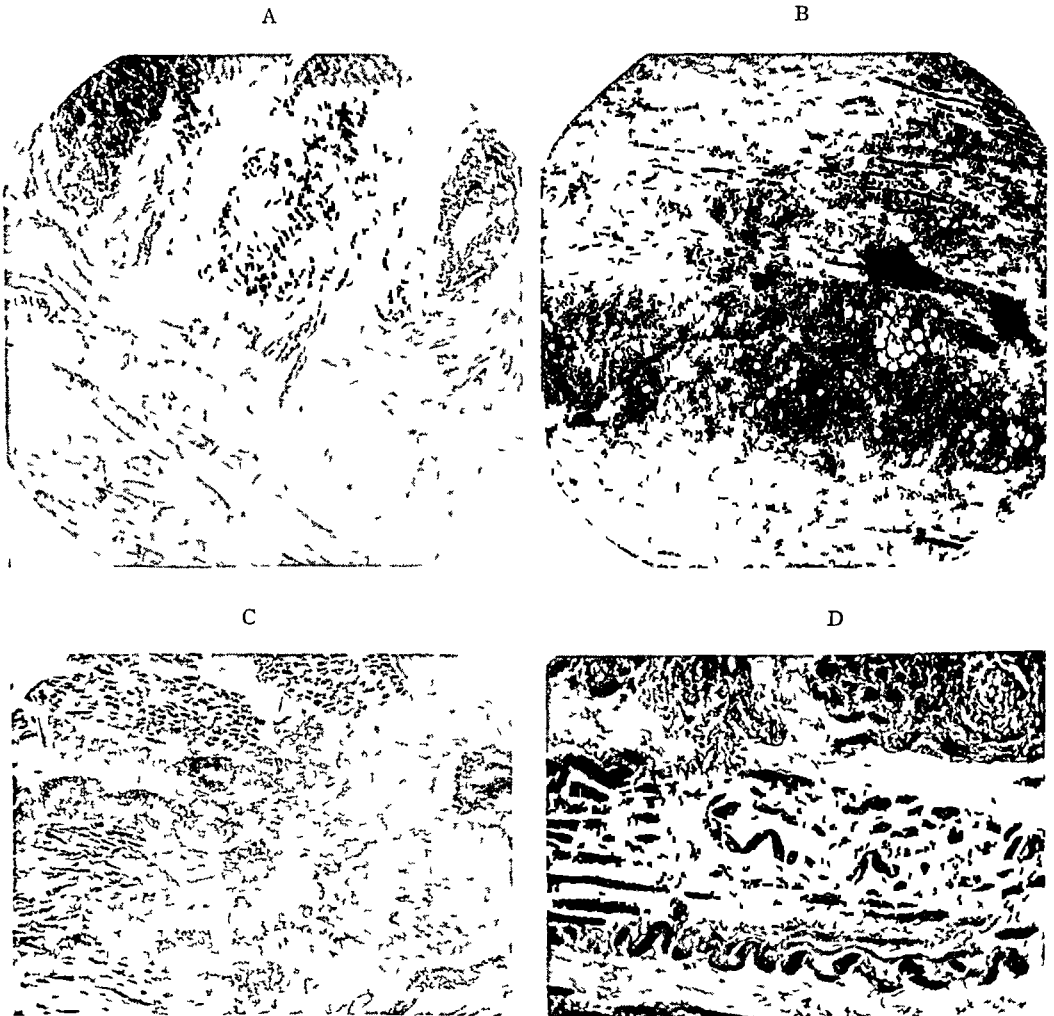


FIG 1 A, B, C, D—Photomicrographs showing pathologic changes in the eye muscles in four of our patients

tion, fibrosis and cellular infiltration. The mildest lesion appears to be a swelling of muscle fibers followed by loss of striation, namely, the early changes associated with so-called Zenker's degeneration. Later, many muscle fibers are seen to be frayed out into a fibrillary substance, which takes the stain for collagen. There is at the same time, in many of the sections, definite interstitial edema. In the more pronounced cases, or perhaps those of longer standing, there is a proliferation of round cells which appears to be coming from the intermuscular mesenchyme. Some of these cells are lymphocytes or immature plasma cells but many are very embryonal in character. Small

and large accumulations are present around the blood vessels. This cellular reaction appears to be, in part, a response to necrosis of the muscle. What appears to be a still later change is the condensation of fibrils into a comparatively dense scar tissue, although in no case can it be said that the condition is resting. One finds early, intermediate and late stages in all of the tissue. In addition to these changes, in some sections the whorls of the arterioles are somewhat thickened and are infiltrated themselves by mononuclear cells. In places, these cells appear beneath the intima causing a slight bulging of the endothelium."

In some of our patients, additional biopsies of muscle were taken from other portions of the body in order to determine whether similar alterations had occurred, but such changes were not found. It is our feeling, however, that they might well be present, particularly in view of such reports as that of Dudgeon and Uiquhait.⁵ These writers reported on lymphorrhages in the muscles in exophthalmic goiter in nine cases. The extrinsic muscles of the eye, muscles of the heart, the deltoid, rectus and biceps muscles were examined. One of the patients suffered from myasthenia gravis in addition to exophthalmic goiter. The lymphorrhages varied from a few cells to a wide tract of mononucleated cells, extending for a considerable distance among the fibers and separating them. In some, both small and large lymphocytes were visible. Among the lymphocytes were scattered a few endothelial and plasma cells. Chronic interstitial myositis, with atrophy of the muscle fibers of varying degrees, was a marked feature. In every case, the muscles of the eye were more severely affected than the skeletal muscles and the heart muscle was the least altered. The thymus gland was large. In three cases it showed the usual microscopic appearance met with in this gland in the presence of exophthalmic goiter. In each case, the thyroid gland was characteristic of exophthalmic goiter. The duration of symptoms in these cases was several years. These authors commented that their pathologic findings in the muscles of patients with myasthenia gravis were exactly similar to those described above and that they had not seen the same alterations in other diseases.

In the light of our experiences, it was of particular interest to investigate the literature for other evidences of myopathies. Basedow noted that in one case "because of retrobulbar tension" the recti muscles compressed the globe and caused an indentation between each one. With such an expression, it seems likely that he may have been dealing with enlarged muscles. Numerous writers have commented upon the finding of myositis and great enlargement of the muscles in cases not apparently associated in any way with thyroid disease. In extreme cases in which enucleation was required, large muscles have been commented upon, as they have been in the course of Kronlein's operation. A large number of pathologic reports from cases of idiopathic exophthalmos have been strikingly similar to those in our cases, although, in ours, the association with thyroid disease was clear. Frequently, following an enucleation, the remaining bulk of muscular tissue within the orbit was

sufficiently large to preclude the use of an artificial eye, or required an additional operation to reduce its volume

The myopathies found in our patients have other special interests. The pathologic changes in the eye muscles are identical with those occurring in the eye muscles of patients with myasthenia gravis. The relation of this disease to disturbances of the thyroid gland and to changes in the thymus have been commented upon by various writers, and the finding of identical alterations in the muscles of our patients may be an additional link in the chain of evidence as to the etiology of these conditions. None of our patients showed recognizable evidence of enlargement of the thymus gland.

Another point which impresses one, in the review of the literature of thyroid disease, is its relation to nervous disorders. In the description of nervous diseases appearing in the course of exophthalmic goiter, one notes the predominance of affections of the cranial nerves controlling the eyes and their movements. More recently articles have appeared under the heading of exophthalmic ophthalmoplegia,^{6, 7} a term applied to a certain group of cases in which there has been no demonstrable disorder of the thyroid gland. There can be little doubt but that the neurologist has frequently sought, in the central nervous system, an explanation for various types of palsies of the eye when myopathy of some of the ocular muscles was responsible. We have observed, and have records of, a large number of patients who had varying degrees of exophthalmos which either was not progressive or did not reach a stage which threatened life and vision, so that operation was not performed. In many of these, the evidence seemed to indicate a myopathy rather than any primary nervous disorder. Some of these gave no evidence of thyrotoxicosis.

While, in most instances, the intensely progressive and dangerous proptosis to which we have applied the term "malignant" had a clear association with a disorder of the thyroid gland and followed operation on this gland, one of our experiences is sufficient to show that this type of exophthalmos may appear under other conditions than following such an operation.

Case Report—A. D., age 39, referred by Doctor Dowling of Providence, Rhode Island, was admitted to the University of California Hospital in June, 1932, with a history of diplopia in December, 1930, for which glasses were fitted. In March, 1931, his difficulty had increased. In June, 1931, exophthalmos of the left eye was noted. A malignant tumor of the orbit was suspected and roentgenotherapy administered. In September, 1931, however, enucleation became necessary, no malignant growth was found, and the pathologic report was chronic inflammatory disease. Two months later, the remaining eye, the right, began to show exophthalmos. At this time, evidence of thyrotoxicosis appeared. The basal metabolic rate was plus 24, and late in the same month a thyroidectomy was performed. In January, 1932, the basal metabolic rate was plus 6. Nevertheless, the exophthalmos progressed and, by September, 1932, vision was blurred and there was swelling of the optic disk to about four diopters, with retinal hemorrhages.

Upon admission to our hospital, in September, 1932 (Fig. 2A and B), the basal metabolic rate was minus 13. There was great retrobulbar resistance. In addition to the retinal hemorrhages, exudate had appeared. The exophthalmometer reading was 31, the visual acuity was 120/200. Movements of the globe were limited and there was

A

B



FIG 2 A B—Case A D Before operation October, 1932



FIG 3—Case A D April, 1938 Compare with Figure 2

contraction of the visual field. Upon elevating the lid, the insertions of the muscles were visible. Operation was performed in October, 1932. There was a reduction of 4 Mm in the exophthalmometer readings while the patient was still in the hospital. The hemorrhages and swelling of the disk disappeared rapidly and there was improvement in visual acuity. Six years later, the patient considered the eye to be completely restored in vision and movement, although it is still more prominent than normal (Fig. 3).

Such an experience indicates that progressive exophthalmos may precede the development of recognizable thyrotoxicosis as well as appear subsequent to it. In this patient there was a progressive exophthalmos, requiring the



FIG. 4—Case D P Before operation January, 1932

FIG. 5—Case D P September 1933
Compare with Figure 4

enucleation of one eye, prior to obvious evidences of thyroid disease, in the remaining eye there was progression during a stage of great thyroid activity, but the progressive exophthalmos continued even after other evidences of thyrotoxicosis disappeared.

Pathologic changes similar to those found in progressive exophthalmos must not be assumed for the ordinary degrees of actual or apparent exophthalmos in thyroid disease. There have been but few opportunities for examination of the muscles under such conditions and no uniformity of opinion has been expressed. Such examinations of muscles are needed badly, but

with the low mortality following thyroidectomy, opportunities for postmortem examination have been infrequent

The operation as previously described by us² does not present any particular technical difficulty and it certainly carries very little operative hazard In

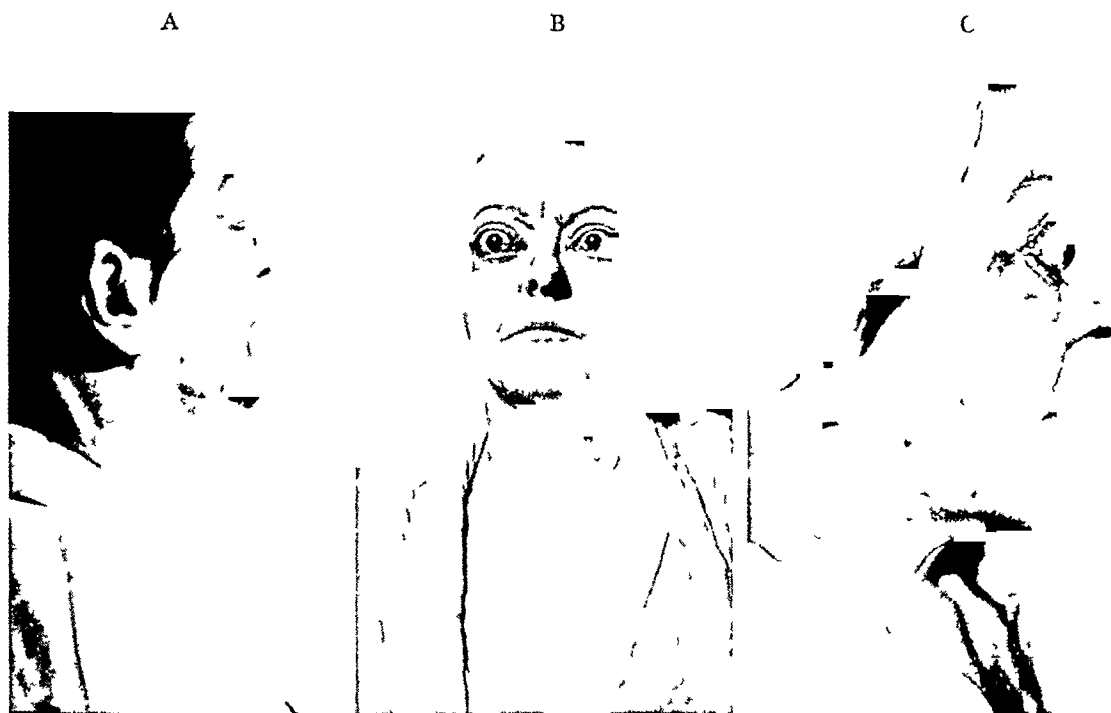


FIG 6 A, B, C—Case S W Before operation, April, 1932



FIG 7—Case S W Immediately following operation



FIG 8—Case S W Ten days after operation



FIG 9—Case S W October, 1933 Compare with Figure 6

almost all of our patients, the bilateral procedure was undertaken at one stage (Fig 12), although the wisdom of this is debatable Following operation, there is immediate recession of the eye The orbital contents show pulsation Shortly thereafter, the orbital contents become edematous and the eyes once more protude During this period of the convalescence, much care is required The degree of edema varies greatly The conjunctivae may have been edematous and protruding from the lids prior to operation In other

instances, such protrusion may appear after operation and be very slow in subsiding. Any lack of vigilance during this period may result in the dying



FIG 10 A, B—Case C H Before operation, June 1936



FIG 11 A, B—Case C H April, 1938 Compare with Figure 10

of the cornea and result in permanent damage. Great care is required. Scrupulous cleanliness, protection of the eyes with a mild boric, ophthalmic

ointment, and prevention of the drying of the conjunctivae. Following this stage, if the decompression has been adequate, the eyes will be found to have receded from 1 or 2 to 6 Mm, in comparison with the condition before operation. Pulsation of the globe is not appreciated by the patient and tends to decrease and disappear. The extent of the decompression is of the utmost importance, for inadequate decompression is likely only to aggravate the condition. Roentgenologic studies of the frontal and sphenoid sinuses and their relation to the orbital plates and optic foramina are always necessary. The distance to which the frontal sinuses extend into the orbital plate varies greatly, and it is most unfortunate when these sinuses are of unusual size, as the area of bony removal in the anterior fossa is restricted by this anatomic

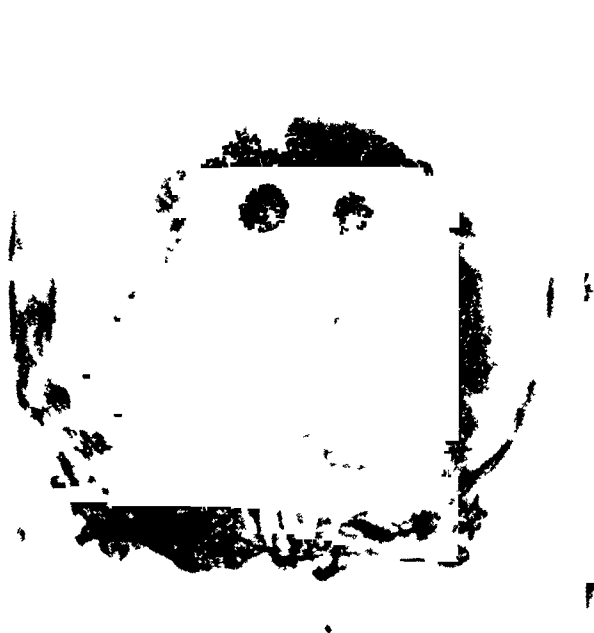


FIG 12—Roentgenogram after operation showing the arrangement of the osteoplastic flaps



FIG 14—Roentgenogram after operation showing optic foramen unroofed

condition. The same is true, to a lesser degree, in regard to the ethmoids. It is our feeling that, in some of our operations—particularly in the one in which the result was poor—our decompressions were inadequate. For that reason, the type of operation has been altered since our previous publication of the surgical technic.² We now remove not only the area of bone over the roof of the orbit, but carry the removal of bone lateralward into the temporal fossa and up close to the orbital rim, removing that portion of the lateral wall down to the antrum (Fig 13). Posterior to this, the removal of bone is continued back into the middle fossa removing the posterolateral portion of the orbit down to, and about, the orbital fissure. When choked disks are present, the optic foramina are unroofed (Fig 14). This does not entail particular difficulty, and the area of decompression is greatly enlarged. Since we have followed this procedure, the immediate recession of the eyes has been much greater and the postoperative hazard lessened.

As mentioned in previous articles, various experimental workers have re-

ported exophthalmos in animals as being produced by drugs and other substances, particularly endocrine products. Such results need to be scrutinized to determine whether or not sympathetic stimulation alone is responsible for the exophthalmos in animals. In many, at least, that have been studied there is a smooth muscle mechanism which, when stimulated through the sympathetic nervous system, is capable of causing protrusion of the eye. In animals, then, overactivity of the sympathetic nervous system is always a possibility as a cause of exophthalmos, and further studies are needed to determine whether or not other factors are involved. In 1909, Karplus and Kreidl⁸ showed that, in cats, stimulation of the hypothalamus, laterally and slightly posterior to



FIG. 13.—Drawing to illustrate the area of bone removed

the infundibulum, caused dilated pupils, wide lid slits and retraction of the nictitating membrane, proving a true hypothalamic center for the sympathetics. A number of workers^{9 10 11 12} have indicated that the injection of anterior pituitary extract is capable of producing exophthalmos apart from any cause acting through the sympathetic nervous system. Particularly significant work has been done by Smelzer¹³ and Marine and Rosen^{10 11}. Experimental work has been carried on in our own laboratory* with similar results. We have been able to produce proptosis by the injection of the thyrotropic hormone as produced by the Junkmann process. For this material we are indebted to Dr Herbert Evans of the University of California. Smelzer recently reported that injections of the thyrotropic, anterior pituitary extract produced exophthalmos in animals from which the thyroid gland and sympathetics had been

* We are indebted to Squibb Company and to Parke, Davis & Company for our supplies of anterior pituitary substance.

removed. He found that the orbital contents became edematous and weighed some 40 per cent more than those of the controls. All of the orbital tissues seemed to participate in this increase in weight, but the extra-ocular muscles in this group weighed some 20 per cent more than those of the controls. He described the tissues as being infiltrated with stainable material, and found the fat to be decreased. Many lymphocytes were present and nests of lymphocytes infiltrated the muscles. He remarked that the microscopic picture is indistinguishable from that in human beings in whom low basal metabolic rates were present. He concluded that the sympathetics have no essential relationship in this process.

Marine and Rosen reported that male rabbits develop exophthalmos more frequently than females. This difference is independent of the thyroid gland, and the exophthalmos develops most frequently in rabbits at about the age of puberty. Gonadectomy greatly reduced the incidence of exophthalmos even in thyroidectomized rabbits. These authors agree that exophthalmos is produced by the thyrotropic hormone and can be caused either by passively introducing this hormone, or by artificially stimulating its production in the animal. Maintenance of normal thyroid activity by the administration of iodine or thyroxin prevents it. They recommended that iodine and desiccated thyroid substance be employed as remedies. It is their hypothesis that a deficiency of some hormone, originating in the suprarenal cortex or gonads, underlies the production of Graves' disease and that the activity of the anterior pituitary is increased by the stimulation of centers in the midbrain.

It is, of course, clear from clinical experience alone that marked and progressive proptosis is not of necessity associated with hyperthyroidism, but more often with hypothyroidism. Sufficient clinical and experimental evidence has been developed to make clear a relationship between these myopathies and other endocrines, and to show that the relationship of the pathologic process to the thyrotropic hormone of the anterior pituitary is intimate.

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DISCUSSION—DR THOMAS M JOYCE (Portland, Ore) I have had two of these patients The first one I saw shortly after Doctor Naffziger's original article appeared, the second one some time later I would like to ask Doctor Naffziger if he has noticed a pulsation in the eyeballs in his patients, which has persisted and has caused considerable inconvenience to the patient For some time this patient had difficulty in reading However, he was able to carry on his work in a garage The second patient looked very much like the photograph that was shown of Doctor Lahey's patient My associate, Doctor Kistner, and I noted in the roentgenogram of her skull that she had an unusually large frontal sinus We took off the inferior plate of the frontal sinus, opened the ethmoid labyrinth and removed the lamina papyracea The edema disappeared and the patient was absolutely relieved of her trouble

Note Since returning home I find that Doctor Kistner has operated upon a second patient which was almost an exact duplicate of this previous case, performing the same operation, namely, removing the floor of the frontal sinus, opening the ethmoid labyrinth and removing the lamina papyracea, with absolute relief

DR MARTIN B TINKER (Ithaca, N Y) This condition is distressing because of severe pain to the patient and, as Doctor Naffziger has stated, many of them go on to commit suicide or to death from natural causes Doctor Naffziger's operation is surely the one indicated in bilateral, severe exophthalmos

Many years ago, a patient upon whom I had operated for exophthalmic goiter returned with a unilateral exophthalmos Exophthalmos had not disappeared after thyroidectomy, and the pain had become very distressing Thinking that there might be intra-orbital pressure, I performed the Kionlein operation, dividing the external angular processes above and below, and the midzygoma, reflecting the wall of the orbit forward to expose the orbital space A tumor the size of the end of the finger was found pressing upon the optic nerve and the eyeball It was removed and the result was entirely satisfactory The exophthalmos disappeared, the pain was relieved and the woman has remained well for many years

This case was reported at the Section of Exophthalmology of the American Medical Association A modified incision was described which was less mutilating than the incision originally proposed by Kionlein The tumor was examined by Doctor Verhoeff, pathologist at the Charitable Eye and Ear in Boston, and was diagnosed as a hemangioma

It would seem to me that there are perhaps a limited number of cases of unilateral exophthalmos giving very distressing symptoms, in which this operation might be indicated The bilateral operation, which Doctor Naffziger has described, seems an extremely valuable procedure, and likely to be needed in many cases

DR HARRY B ZIMMERMAN (St Louis, Minn) Doctor Naffziger has associated my name with a paper referring to this procedure that was published by Dr Frank Birch of St Paul, about the time that this condition first was demonstrated by Doctor Naffziger, probably a little bit before

The patient, a male, had had a thyroidectomy performed, and shortly afterward developed a unilateral exophthalmos of the right side When he came under Doctor Birch's observation, the left eye had begun to protrude very slightly He had a measurable exophthalmos on the left side, but that was not apparent except by actual measurement

A diagnosis was made of a malignant bulbar tumor, and Doctor Birch and I performed the Kionlein procedure of opening the external plate of the orbit The tumor immediately presented itself It was a weird looking tumor, rather diffuse, and consisted of the extra-ocular muscles bulging out into this defect in the external wall of the orbit, a sort of watery, edematous looking muscle The muscles were incised, and it seemed an interminable procedure to get through the greatly thickened tissue, which was at least almost half an inch thick That apparently formed the entire tumor, and consisted solely of the enormously thickened, edematous extra-ocular muscles

The orbit was decompressed by this procedure The histologic section of the hyperplastic muscles was a good deal as Doctor Naffziger has described The procedure was stopped We had some slight regression because of the decompression of the external wall of the orbit, but nothing such as would have been accomplished had the decompression been made as Doctor Naffziger described

The condition progressed to destruction of that eye, which was eventually removed, by which time he had a loss of the other eye by a similar process That was the first time it came to my mind that these exophthalmoses were due to this peculiar thickening and hyperplasia of the extra-ocular muscle

DR FRANK H LAHEY (Boston, Mass) I think it is important to bring out a fact which has not been entirely accepted, and that is that resections of the superior cervical sympathetic ganglia do not produce exophthalmos Such resection does produce droop of the lid and we have repeatedly utilized it to improve the appearance of some of these patients who have wide palpable fissures It is, I think, from that point of view, a valuable procedure

We have had, however, one complaint in connection with that operation and that is that many of these patients who have had resections of their superior cervical ganglia complain of a disagreeable dryness in their nose

I would like to ask Doctor Naffziger if he has had to utilize suture of the lids, because some of these problems in our hands are pretty acute

These patients who come in with edema of the conjunctiva are candidates, as you know, for slough When you realize that the conjunctiva is nourished by osmosis and not by vascularization, it needs only a little increase in lid pressure to produce a slough of the eye covering

I think, therefore, it is extremely important that you are dealing with intractable exophthalmos to be aware of this danger when you see a wrinkling of the conjunctiva It has been our experience, and it has been Doctor Horrax' experience as it has been Doctor Naffziger's, that better results have been obtained when more of the bony orbit is unroofed and when the excision is carried down over the outer angles

DR HOWARD C NAFFZIGER (closing) With reference to pulsation of the globes immediately after operation, this is present at once, but gradually lessens and ultimately disappears The patients are not conscious of it We

have assumed that a new fibrous covering replaces the peri-orbita and prevents the transmission of diurnal pulsation

Diplopia may occur after operation because of the herniation of muscles through the decompression, which temporarily hampers and restricts their movement

Apparent unilateral exophthalmos associated with thyroid disease is not uncommon. Careful observations have indicated, however, that there is usually some slight degree of exophthalmos in the less prominent eye. In other words, the exophthalmos of thyroid disease is usually bilateral, though there may be marked asymmetry in the degree of protrusion of the two eyes. A purely unilateral exophthalmos is more characteristic of orbital tumor.

The Kionlein operation has been performed for malignant exophthalmos but is inadequate for these severe cases.

Many patients have an unsightly but not dangerously progressive exophthalmos. In these, the widened lid slits need correction more than the proptosis does. This is readily observed by pinching the lids together at the outer canthus, so as to narrow the palpebral fissure; the appearance is greatly improved. Advancing the external canthus by suture is easily performed.

INJURIES TO THE RECURRENT LARYNGEAL NERVE IN THYROID OPERATIONS

THEIR MANAGEMENT AND AVOIDANCE

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AN INJURY to one recurrent laryngeal nerve during the course of a thyroid operation is an unfortunate incident and an injury to both recurrent nerves is a really serious surgical calamity. Because of the fact that injury to both nerves does not as a rule produce any immediate emergency even though the ultimate results occasion real and crippling disability, also because of the fact that injury to one recurrent nerve causes only temporary loss of voice and usually no limitation in breathing, there has not been as active an interest in the methods for lessening the number of injuries to these nerves as seems desirable.

Thyroid surgery is now so well established upon such a sound basis and with such a low mortality that the operation is being more often accepted by patients and more frequently performed by an increasing number of surgeons. That there is a real need for all of us to interest ourselves in diminishing this incidence of injury to recurrent nerves is established by the fact that even though our percentage ($1\frac{1}{2}$ per cent) of nerve injuries is but one-half of that reported by several other writers (3 per cent), it represents a largely avoidable catastrophe in a great number of patients.

The prevailing attitude of surgeons toward the recurrent laryngeal nerves has been one that has been handed down, unchanged, from the beginning of our experience with thyroid surgery. Kocher, the father of thyroid surgery, advocated partial thyroidectomy under local anesthesia because he could ask the patient to speak and thus know that the recurrent nerves were not injured. This as we now know was not a sound position since in some patients in whom the recurrent nerve has been injured there is not an immediate and striking change in voice. In many patients, immediately after and probably during thyroid operations, there are temporary voice changes without injury to the recurrent nerves. If there is a voice change demonstrating an injury to the nerve, the damage has been done. It is much better to dissect and visualize the nerve and thus avoid its injury. We have all for many years unquestionably accepted what amounts to unsubstantiated impressions about the recurrent nerves, some of which are here recorded. That the recurrent nerves are too small to dissect and demonstrate, that dissection and manipula-

tion, if accomplished, would result in a high percentage of recurrent nerve paralyses, that direct suture of cut recurrent nerves was not worth undertaking because it was thought impossible to find the injured nerves in the scar tissue which forms following subtotal thyroidectomy. It has also been assumed that if the nerves were found, they were too small to be successfully sutured. Because of the above facts it has been considered desirable in thyroid operations not to see recurrent nerves and to avoid seeing them by leaving sufficient strips of thyroid tissue over the nerves so that they would not be visualized.

Some three years ago, one of us (F. H. L.) undertook to demonstrate the recurrent laryngeal nerve in practically all* thyroid operations. This policy has been accepted by all the surgeons in the clinic operating upon patients with thyroid disorders. As a result of this experience, now amounting to well over 3,000 dissections of the nerve at this time, all of the above impressions have been proven to be incorrect. The nerve is of sufficient size so that not only can it easily be dissected but it has sufficient body so that it can be readily palpated as it is pushed laterally against the rigid tracheal wall. It has been demonstrated that routine dissection and demonstration of the nerves and even palpation while on a moderate stretch cause no immediate or late interference with their function. Three nerves previously cut before the patients came to the clinic have been found and accurately and easily sutured. What the eventual outcome will be in these cases done six months and three months ago cannot now be stated. It has been definitely proven, however, that cut nerves can be found and can be sutured without great technical difficulties. As the result of exposing at least 3,000 recurrent laryngeal nerves in a period sufficiently long (three years) to permit late complications to occur if they were to occur, it may be said that the routine exposure of recurrent laryngeal nerves in thyroid surgery is a safe and justifiable procedure and will diminish, if not largely eliminate, injuries to that nerve †.

There have been so few writings and discussions concerning recurrent laryngeal nerve paralyses and the clinical features evidencing this state, that there tends to be considerable confusion about it. One is that if both recurrent laryngeal nerves are injured, there will be immediate difficulty with breathing while the patient is still upon the operating table. Under certain circumstances, later discussed, we believe it is possible for such a respiratory emergency to arise but it is by no means the usual course of events. The clinical history of a patient whose recurrent laryngeal nerves have been interrupted is as follows. During the operation itself, there is usually very little difficulty with the patient's breathing but immediately following operation the patient finds himself unable to talk, due, of course, to the cadaveric position of both cords and the patient's inability to tense them, caused by their

* There will be occasional very ill patients with hyperthyroidism in whom it may prove difficult to find the nerve and in whom the saving of time will be of greater importance than the demonstration of the nerve.

† Up to three years ago the incidence of recurrent laryngeal paralysis was 1.6 per cent. During the last three years, under the above plan, this has dropped to 0.3 per cent.

loss of enervation Within six months' time, this patient frequently reports to the surgeon quite elated with the fact that her voice is returning and unless the surgeon is familiar with the usual course of events, he too may be elated In a few months more, however, the patient returns still able to talk but complaining that she is less and less able to breathe satisfactorily, particularly after any unusual activity This state of affairs progresses still further until, due to the insufficient air-way in the permanently narrowed glottic space,

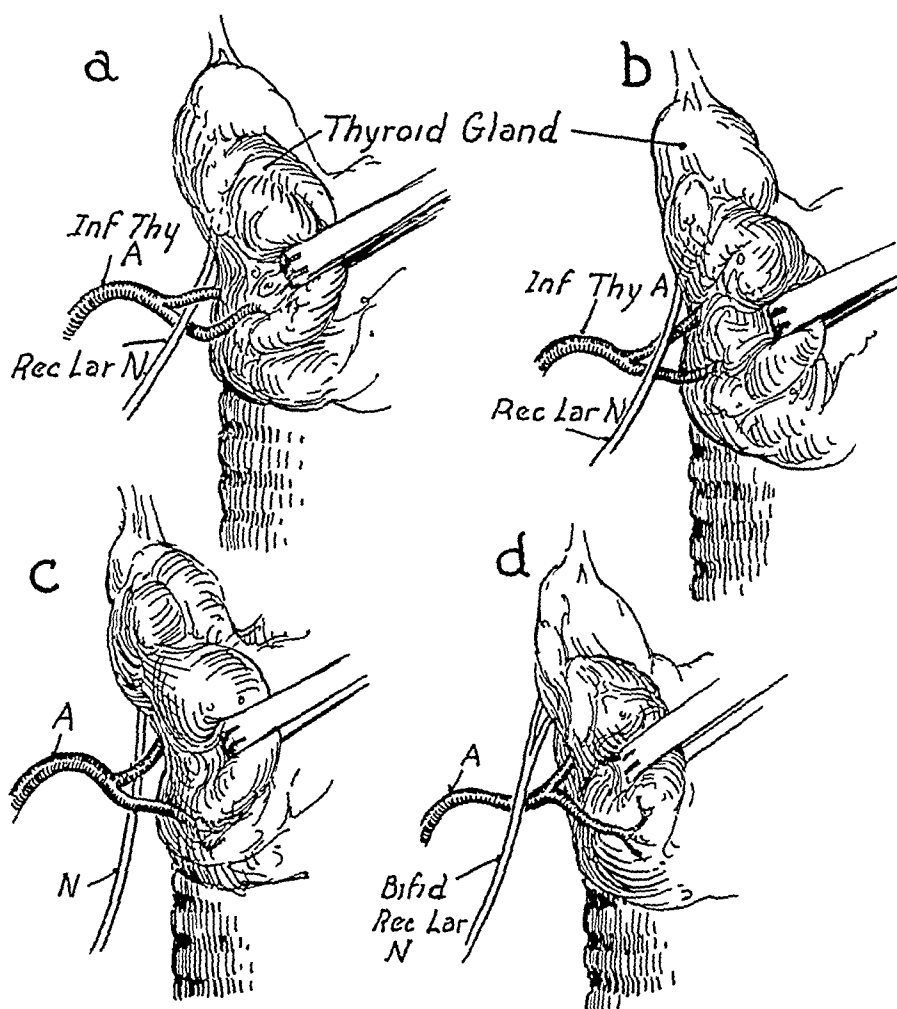


FIG 1—Variations in the relationship between the recurrent laryngeal nerve and the inferior thyroid artery encountered in operations on the thyroid

(a) An uncommon relationship the nerve passing over one branch of the inferior thyroid and under the other

(b) Not the rule, but a not uncommon relationship the nerve passing entirely anterior to the artery

(c) By far the most common relationship the nerve passing entirely posterior to the artery

(d) A not uncommon division of the nerve before entering the larynx

there is difficulty with breathing on any exertion, even slightly beyond the most moderate

An additional sign at this time evidences itself also, that is, inspiratory crowing An excellent way to demonstrate the effect upon breathing of the fixed cords and narrowed glottic space is to ask a patient with bilateral abductor paralysis to count to the highest possible number without taking a breath It will be found that when the patient has counted from between

15 to 25, a long inspiration will be necessary which, because of the attempt to take in a considerable amount of air, will cause the typical inspiratory crow so characteristic of bilateral abductor paralysis. There is also a characteristic "roaring" during sleep.

A condition under which interference with breathing may conceivably take place during operation would be in a patient most of whose recurrent laryngeal nerves divide extralaryngeally into the abductor and adductor fibers, as shown in Figure 1 d, and in whom only the abductor fibers of the nerve were

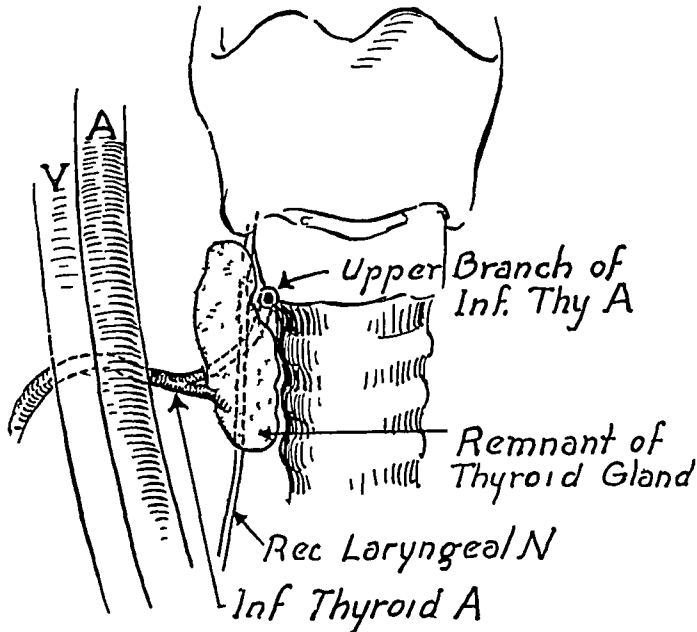


FIG 2—Showing the relationship of the recurrent laryngeal nerve, before it enters the larynx, to the upper branch of the inferior thyroid artery. This is depicted diagrammatically as seen from above as it is in a subtotal thyroidectomy. Attempts to snap this bleeding branch in its position between the thyroid and the trachea can result in injury to the recurrent nerve.

The arrow points to the trunk of the inferior thyroid artery, at which point it should be ligated for bleeding of the upper branch of the inferior thyroid artery, rather than attempting ligation of the bleeding vessel itself.

injured is just below that point where the nerve passes under the lower fibers of the inferior constrictor muscle to become intralaryngeal (Fig 2).

We have rarely seen injuries to the recurrent laryngeal nerve at the level of the inferior thyroid artery. Anatomically at this level the nerve (Fig 1), which passes obliquely inward toward the trachea, is usually at some distance from the gland, while at the upper level the nerve is either in contact with that portion of the thyroid gland which rests against the cricothyroid junction or even runs through the thyroid substance at this level (Fig 2).

We feel very sure that one of the frequent causes of injury to the recurrent laryngeal nerve is the fact that the upper branch of the inferior thyroid artery at this point, as shown in Figure 2, is located between the thyroid gland and either the upper part of the trachea or the cricoid. This vessel is frequently torn off at this point in subtotal thyroidectomies and retracts beside the trachea below the level of the stump of thyroid tissue left behind as the thyroid remnant. One will observe in illustration that if attempts were to be

injured at the upper pole. Should this unusual anatomic condition be combined with an unusual bilateral surgical accident in which the injury occurred selectively only in the abductor portion of the bifid nerves, immediate narrowing of the glottic space with difficulty in breathing could then take place.

As the result of an extensive experience with recurrent laryngeal nerves and also based upon the experience which we have had in demonstrating injuries to recurrent laryngeal nerves, we believe that the point at which most recurrent laryngeal nerves are

made to catch the bleeding end of this vessel, as it retracts between the stump of thyroid tissue and the trachea, the hemostat would frequently be carried well down beside the trachea so that when it catches the bleeding vessel, it may also catch the trunk of the recurrent laryngeal nerve just before it penetrates the constrictor fibers to become intralaryngeal.

We have frequently demonstrated the point of bleeding from this vessel branch by putting a closed hemostat down between the trachea and the remnant of thyroid tissue and then turning the remnant of thyroid tissue inward

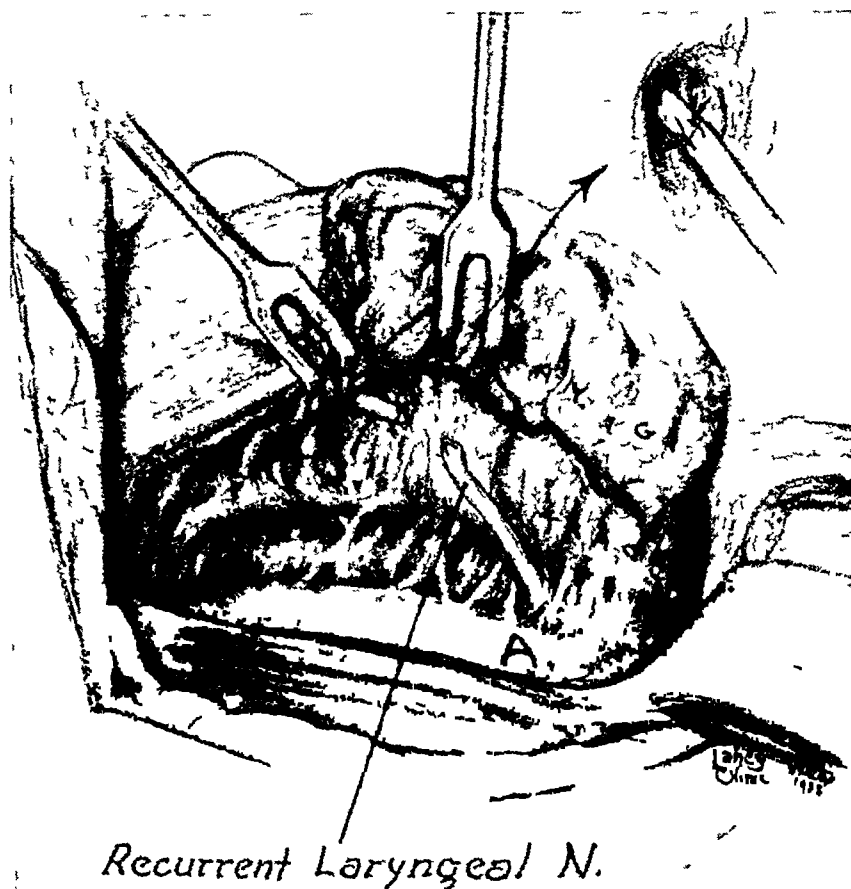


FIG 3—This and Figure 4 were drawn at the operating table to demonstrate the location and suture of the recurrent laryngeal nerves in two cases. The nerve had been severed just below the point where it entered the larynx. Note the black silk ties found on each end of the severed nerve. The insert illustrates the fine black silk vessel sutures inserted on either side of the approximated nerve to oppose fibers conveying similar impulses.

With the recurrent nerve visualized, the close proximity of the nerve to this bleeding point, and the danger of injury to the nerve at this level, become clearly apparent. We feel very sure that technical difficulties with bleeding at this level, which are by no means uncommon, are the cause of many injuries to recurrent laryngeal nerves. Should bleeding occur from the upper branch of the inferior thyroid where it is located close to the trachea at this level, as shown in Figure 2, it is best controlled not by attempting to find the bleeding point but by ligating the trunk of the inferior thyroid artery as it comes up from behind the common carotid at some distance from the nerve, thus protecting the nerve from the danger of injury (Fig 2). This, we feel

certain, is a valuable and practical point in protecting recurrent laryngeal nerves against possible injury

Our attitude, and the attitude of surgeons in general, toward injuries to the recurrent laryngeal nerve has, we believe, up to the present been quite wrong. We, as has everyone else, have assumed that if one or both recurrent laryngeal nerves have been injured or cut, nothing can be done about it. Much of this attitude we believe is a traditional one based upon the assumption that severed or injured recurrent laryngeal nerves could not be found and could not be successfully sutured. This we have proven to be erroneous. In an instance (Figs 3 and 4) in which both recurrent laryngeal nerves had been severed elsewhere ten months previously, the proximal stump on one side having retracted intralaryngeally, both nerves were successfully found and

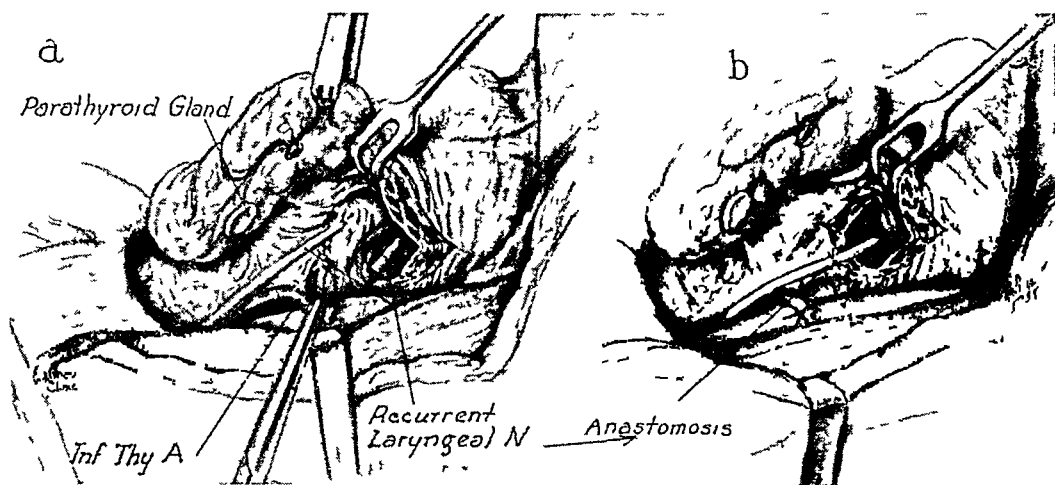


FIG 4—(a) The upper end of the severed recurrent nerve had retracted beneath the fibers of the inferior constrictor muscle. Note the black silk tie found on the lower end of the severed nerve. The retracted upper end of the severed nerve was demonstrated by incising the lowest fibers of the inferior constrictor muscle.

(b) Suture of the nerve by two fine silk sutures, attempting to keep abductor and adductor fibers together.

anastomosed without difficulty and without tension with No. 16 China silk on blood vessel needles. In addition to this, in a recent case in which the nerve had also been severed elsewhere, some years previously, in which reoperation in our clinic became necessary because of a recurrent hyperthyroidism, after the removal of the remnant of thyroid, the severed nerve was sought for, both ends were easily found and reunited, merely for the purpose of establishing the technic but with, of course, no prospect of a return of function because of the lateness of the anastomosis.

If we are to successfully reunite severed recurrent laryngeal nerves so that there is a possibility of restoring function to the vocal cords, the operation must be performed, we believe, within three months of the time of injury. It must be appreciated that in late operations, undertaken to resuture injured recurrent laryngeal nerves, not only is there the diminished likelihood of nerve regeneration but also fixation of the arytenoids may well occur. Also, atrophy and fibrosis of the laryngeal muscles may take place, so that even though

impulses pass successfully along the recurrent nerve to the arytenoidius lateralis and the arytenoidius posticus muscles, the fibrotic shortening of the interarytenoid may well prevent the cords from being separated

As the result of our experience in demonstrating nerves and also because of the ease with which they can be found and approximated, particularly when one makes use of the Berens' binocular loupe, which magnifies the field of vision and the size of the nerve two and one-half times, we believe that in all patients with an injury to a recurrent laryngeal nerve which does not disappear in three months, the nerve should be explored and if injured, the injured section removed, and if severed, the ends refreshed and anastomosed. Delays beyond this time quite definitely jeopardize the probability of a success. Should no injury be demonstrated, exploration will have done no harm, and the patient will have been given the opportunity to recover cord function which might otherwise be completely lost.

When searching for the ends of recurrent laryngeal nerves which have been previously cut, all vascular and scar tissue attachments of the stump of remaining thyroid remnants should first be completely severed from their connection with the internal jugular vein and common carotid artery. The stump of thyroid tissue is then grasped with double hooks, rotated inward and the inferior thyroid artery identified. This is the landmark by which the lower section of the severed nerve may be found as it passes either under or over this vessel as shown in Figure 1 *a*, *b* and *c*. With the aid of the Berens' magnifying loupe, and with a good light brightly illuminating the field, and with care and patience, the stump of the nerve can be found without great difficulty. Since most of the injuries to recurrent nerves, which we have seen, have been close to the point where the nerve enters the larynx, the nerve will usually be found intact at the point where it is in relation to the inferior thyroid artery. The Berens' magnifying lenses, which have a sufficient focal range so that structures can be visualized without danger of the lenses contaminating the field, have for many years proven very useful to us in finding parathyroid bodies, and are especially useful in demonstrating the longitudinal striations of the nerve, thus differentiating it from small veins which can easily be mistaken for it.

The landmark by which the upper section of the severed nerve is found is the horn of the thyroid cartilage. It is just posterior to the point where that structure (thyroid horns) is in contact with the cricoid where the nerve passes beneath the lowest fibers of the inferior constrictors to become intra-laryngeal. Unless the nerve has been severed, as happened in one of our cases (Fig. 4), so close to the point where it entered the larynx that it retracts beneath the inferior constrictor, it can usually be demonstrated by finding its point of entrance into the larynx. When the nerve has so retracted, as illustrated in Figure 4, the plan of cutting some of the lowest fibers of the inferior constrictor as suggested by Dr. Charles Frazier, and indicated in Figure 4, will make it possible to find the retracted upper end of the nerve intact beneath the muscle fibers. When found at this point the upper end in

our case possessed enough slack so that it could be pulled down for at least a half inch and was uninvolved in scar tissue

One of the difficulties of suture of recurrent laryngeal nerves is that of approximating abductor fibers with abductor fibers and adductor fibers with adductor fibers, as it is a nerve carrying impulses to opposing muscles. Since we are as yet able to present only cases in which recurrent nerves have been found and satisfactorily sutured and cannot as yet present proven return of function, we are unable to say whether or not successful restoration of double impulse nerve conduction in a single trunk can ever be successfully accomplished. It may be possible that it will never be effected in humans. One should, however, in anastomosing recurrent nerves, make every effort to unite the nerves so that there is at least a reasonable chance of fibers conveying similar impulses being opposed to each other. When the nerve is visualized through the magnifying lenses it can be seen that it is somewhat flattened, and in uniting it, one should be careful to place the fine silk vessel sutures along the outer and inner margins of the nerve (Fig 3), one on either side, so that the two ends of the nerve are united in the same flat plane and with no twist in them.

There has been so little experience reported of the surgical approach to this nerve that we can draw only upon our own in discussing what great defects may exist as the result of scarring or excision that require removal of segments of the nerve and still enable one to approximate the cut ends without undue tension upon the nerve and the delicate sutures which unite its severed ends. In the last case in which direct anastomosis was performed, at least a half inch of the nerve was involved in scar tissue and had to be sacrificed. In spite of this loss, the ends could be easily approximated and sutured. The course of the recurrent nerve is obliquely inward toward the trachea. When the nerve passes in front (unusual) of the inferior thyroid artery, there is considerable slack in it. When it passes behind the inferior thyroid artery (its common position), its inward oblique course is somewhat angulated. Severing the inferior thyroid artery between ligatures permits liberation of the nerve from this angulation and provides considerably more length of nerve with which to bridge the defect.

We have, so many times, palpated the nerve, however, when the lobe of the thyroid has been inverted and found it under slight tension, that we doubt very much if it will be possible to make the ends come together when more than one-half to one inch is lost.

If a sufficient section of the nerve has been destroyed so that the procedure physiologically most likely to be successful (direct end-to-end anastomosis) cannot be employed, then, based upon surgical experiences with other nerves, one of two procedures must be resorted to—either the insertion of a nerve graft after the plan proposed by Duell and Ballance in which a section of the distal portion of a nerve which has designedly been cut and permitted to degenerate is inserted, thus serving as a tube along which nerve fibers may

RECURRENT LARYNGEAL NERVE INJURIES

grow, on the attachment of the end of a foreign nerve to the refreshed proximal end of the recurrent nerve

This latter procedure was proposed and practiced by Dr Charles Frazier, who employed the anastomosis of the descending branch of the hypoglossal to the cut recurrent laryngeal nerve, but offers, we believe, little chance of success since the impulses habitually passing down the descending hypoglossal are in no way coordinated with the impulses of respiration. A better chance

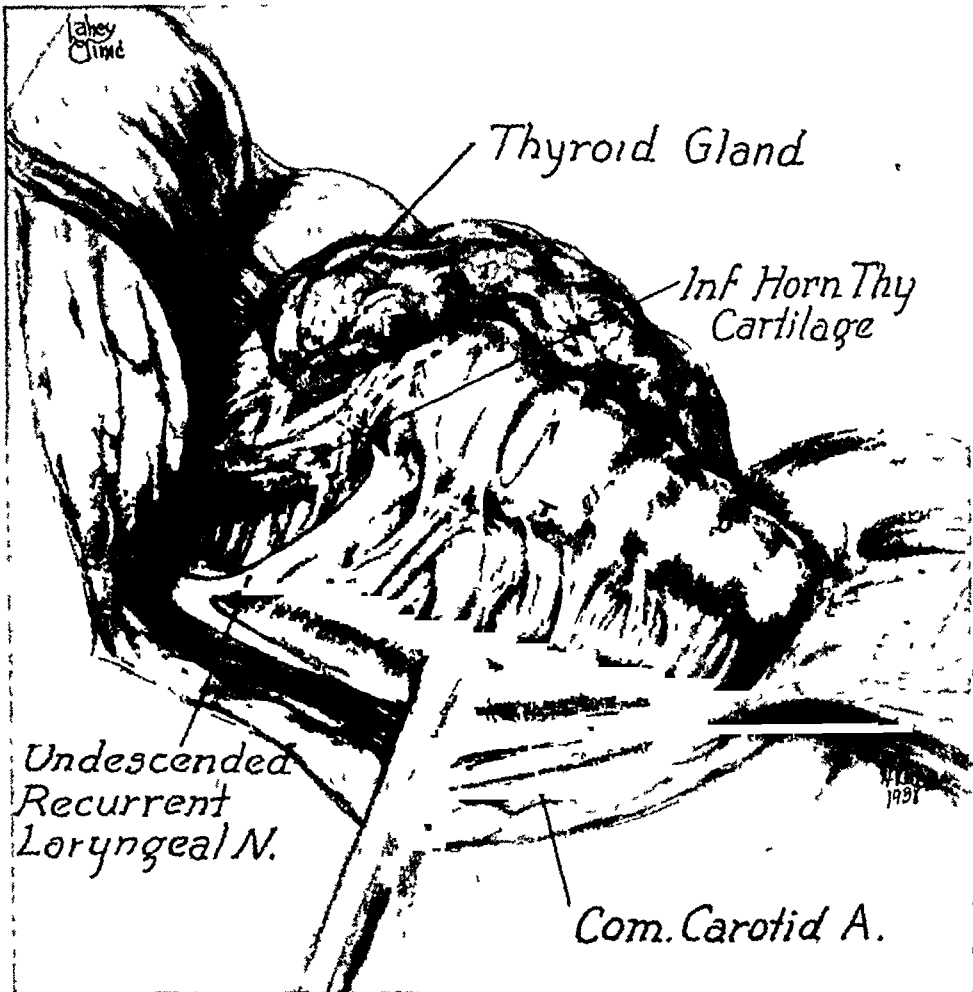


FIG 5—Nondescent of the inferior laryngeal nerve. Note how easily such an undescended nerve could be injured if its course were not demonstrated surgically.

for success exists in carrying out the suggestion, made by Mr Lionel Colledge and Sir Charles Ballance, that a section of the phrenic nerve be anastomosed to the proximal end of the severed recurrent laryngeal nerve, since the respiratory impulses passing down this nerve are coordinated with the impulses constantly passing down the fibers of the recurrent laryngeal nerve. These two investigators, several years ago, performed interesting experiments upon animals relative to the suture of foreign nerves into the cut end of the recurrent laryngeal nerve, and obtained more evidence of a return of function when the phrenic nerve was employed than with the use of any other nerve.

A condition by no means common, but occasionally occurring, is the non-

descent of the recurrent laryngeal nerve Figure 5 illustrates an instance of such a nondescended inferior laryngeal nerve, which occurred in our own experience Many anatomists have written on the subject of the nondescent of the inferior laryngeal nerve and a few surgeons, including Dr John deJ Pemberton, have described the occurrence of such an abnormality in the recurrent laryngeal nerve

In the case illustrated by Figure 5, it will be seen that the nerve passes straight across from the vagus to enter directly under the lowest fibers of the inferior constrictor It will be obvious, in this situation, that if the recurrent laryngeal nerve is not dissected this abnormally located nerve will frequently be caught in ligatures of the upper pole, if, on the other hand, the nerve is sought for as we have advised and is not found, the vagus will be investigated, and this abnormality demonstrated and the nerve thus protected from injury

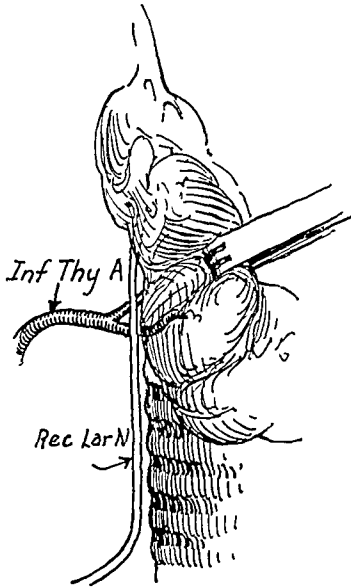


FIG 6—The type of displacement of the recurrent nerve toward the trachea which takes place in deep intrathoracic goiters This is the type of displacement of the nerve commonly found in intrathoracic goiters, and was found to be intact after removal of the intrathoracic goiter shown in Figure 7

In our early experiences with large and deep intrathoracic goiters, we were quite apprehensive that their removal would result in a high percentage of recurrent laryngeal nerve injuries, on the assumption that there was such an anatomic distortion of the course of the nerve by the large intrathoracic extensions that they would be frequently injured when these deep goiters were roughly extricated from the mediastinum This has not been the case and repeated dissection and demonstration of the recurrent nerve, after removal of deep intrathoracic goiters, have shown that such distortion of the course of the nerve as does occur, is in a safe direction, displacing the nerve inward against the trachea (Fig 6), where it is quite safe from injury during the removal of an intrathoracic goiter even of one of such size as is shown in Figure 7

Thyroid operations have been responsible for 35 instances, or 90 per cent, of bilateral abductor paralysis which have been studied in the Lahey Clinic In 15 patients, paralysis was temporary and function of one or both vocal cords was recovered In 20 cases, paralysis was permanent, and of these only one occurred following operation in this clinic The remainder had been produced elsewhere

Permanent bilateral abductor paralysis is a real calamity to the individual, because of the marked obstruction of the larynx by the mesial position of the vocal cords, especially on inspiration We advocate in this condition the employment of a tracheotomy cannula when a patient's activity is limited by want of air A tracheotomy tube, fitted with a Tucker valve, permits these patients to retain an excellent voice without the inconvenience of having to place the finger over the tracheotomy opening while speaking This is a



FIG 7—Anteroposterior and lateral roentgenogram showing an intrathoracic goiter so deep and so large that its removal could be successfully accomplished only after removal of the inner half of the clavicle and the manubrial portion of the sternum. Dissection of the recurrent laryngeal nerve in this case, as in many other cases of intrathoracic goiter shows the only distortion of the course of the nerve to be in an inward direction against the trachea (Fig 6) where it is less likely to be injured by the removal of the intrathoracic extension than when in its normal position.

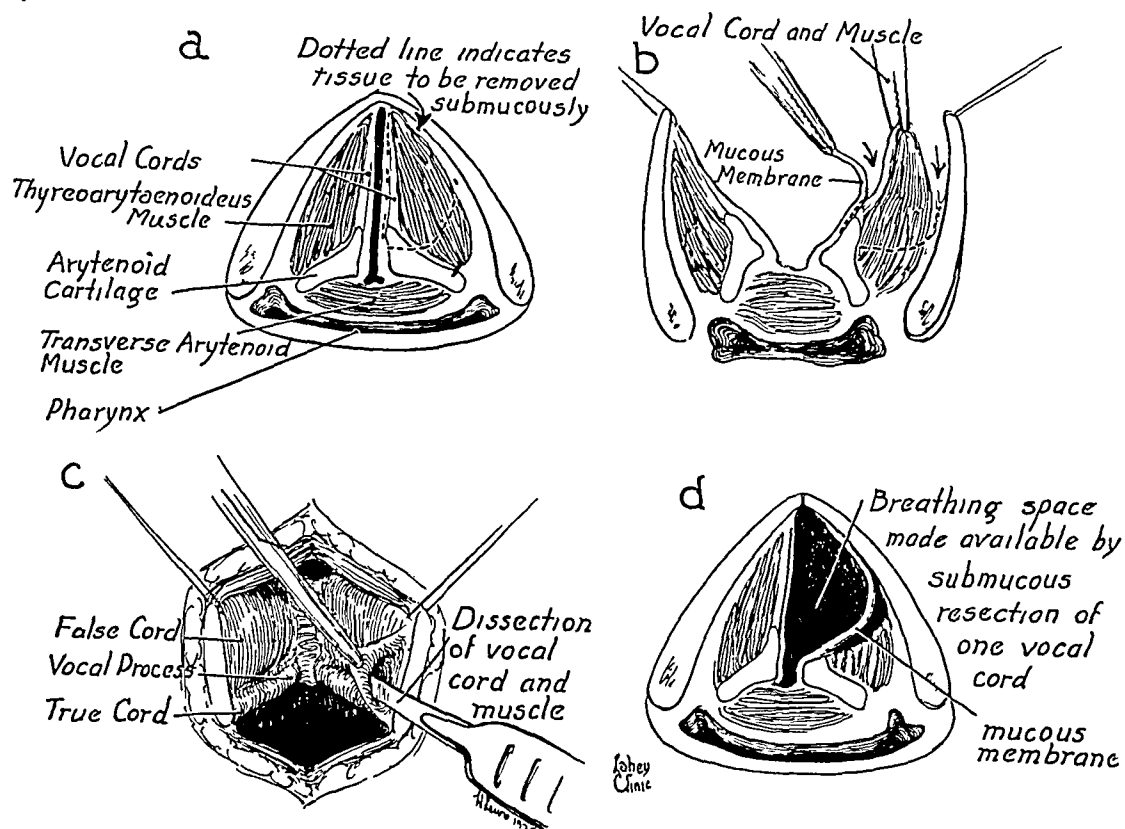


FIG 8—Submucous Resection of a Vocal Cord for Bilateral Abductor Paralysis (Hoover)
(a) A diagrammatic cross section of the larynx in a patient with bilateral abductor paralysis with the median laryngofissure not yet made. Note the area of vocal cord to be resected submucously, demonstrated by the dotted line.
(b) The median laryngofissure made. The mucous membrane in the tip of the hemostat lifted from the cord and muscle.
(c) A front view through the laryngofissure of the dissection of the mucous membrane from over that portion of the cord and muscle to be removed.
(d) A diagrammatic cross section of the larynx with the laryngofissure closed, showing the cord and muscle removed submucously, the mucous membrane pushed back against the laryngeal wall where it is held with gauze packing until it has adhered to the wall and serves as a mucous membrane lining for the enlarged glottic space indicated as breathing space and shown in black.

valuable asset to teachers and saleswomen who depend upon their voice for a living

A few patients, however, do not become adjusted to the permanent use of a tracheotomy tube and desire to sacrifice their excellent voice for a hoarse voice or whisper if they can but breathe without a tube. In such individuals the submucous resection of a vocal cord is recommended. Eight of the 20 patients with permanent paralysis have been operated upon by this method. The technic of the operation has been previously described by one of us¹ (W B H). A preliminary tracheotomy is performed and followed in five days to one week by median laryngofissure, which gives good exposure of the vocal cords. The mucous membrane is then elevated with a sharp knife over one true vocal cord and above and below the cord as well. The muscle is separated from the cartilage laterally. The muscle is then cut off posteriorly, also the vocal process of the arytenoid is removed. Bleeding is controlled. The mucous membrane is now placed against the lateral wall of the larynx and held in place by an iodoform gauze pack (Fig 8). The larynx is closed and the pack removed from five days to a week later.

Healing is rapid because there are no raw surfaces to granulate and cicatrize, and the operation leaves an open glottis and an ample air-way. The voice is impaired and is hoarse, comparable to the voice resulting from removal of a vocal cord in cases of carcinoma of the larynx.

In six of the eight cases the results have been quite successful. One patient was infected at the time of operation by vomiting and was not improved. The first patient operated upon was markedly benefited.

As the result of the experience which we have now had with this method of relieving laryngeal obstruction due to bilateral nerve injuries, we feel that the 75 per cent excellent results, obtained up to now, can be still further improved.

CONCLUSIONS

Routine dissection and demonstration of the recurrent laryngeal nerves in thyroid surgery have proven a safe and valuable method of protecting that structure from operative injury, lowering the incidence of nerve injury in three years from 16 to 0.3 per cent.

The nerve is of sufficient size to be palpable in many cases.

Dissection and demonstration of the cut ends of accidentally injured or severed recurrent laryngeal nerves, together with accurate suture, is a relatively simple and a very feasible surgical procedure.

Exploration of the recurrent nerves, where injury to these structures has occurred, should be undertaken within three months of the injury if one is to hope for possible restoration of function.

Nondescent of the inferior laryngeal nerve is reported, and such a case illustrated. Other anatomic variations are illustrated.

The advantages of the employment of the phrenic nerve, when foreign nerve anastomoses are considered, are suggested.

A plastic operation on the larynx is described and illustrated which, in six out of the eight cases in which it has been employed, has been successful, by permitting closure of the permanent tracheotomy opening and by providing a natural an-way through the larynx adequate in caliber for any degree of exertion

REFERENCE

- ¹ Hoover, W B Bilateral Abductor Paralysis, Operative Treatment by Submucous Resection of the Vocal Cords Arch Otolaryngol, 15, 339-355, March, 1932

DISCUSSION —DR WALTER B HOOVER (Boston, Mass) Doctor Lahey has said very little about the result of cutting one recurrent laryngeal nerve, and I would like to explain what happens when one recurrent laryngeal nerve is cut, or injured Usually, there is hoarseness or loss of voice immediately following the section of one recurrent laryngeal nerve, with the loss of function of this one cord Occasionally, however, the injured cord will lie in the midline of the larynx and there will be no loss of voice, even though one cord is paralyzed Ordinarily, however, the loss of the function of one cord results in a temporary loss of voice, which lasts from a few days to several months, but one can say almost certainly, that the loss of one recurrent nerve will not result in any discomfort to the patient as far as respiration is concerned, and we can assure the patient that the voice will return, because the cord will eventually come to the midline and will get a very good tension in it with a resulting good voice This happens no matter what treatment is, or is not, used

Therefore, we can say that the treatment of the section of one recurrent laryngeal nerve or the loss of function of one cord is that of reassuring or comforting the patient, rather than any other treatment

Permanent bilateral abductor paralysis is a major catastrophe, because the patient cannot sleep at night, or if he does sleep, is annoying to anyone nearby The patient is short of breath and cannot exercise, and is truly an invalid, often depressed and despondent Anyone who has had his activities limited because of bilateral abductor paralysis should have a tracheotomy tube placed A tracheotomy tube is a safe and certain method of establishing an airway, and every patient, whose respirations are limited or whose activities are limited for want of air must have this done

The tracheotomy tube should be placed at least as low as the second ring of the trachea so that perichondritis and cicatricial stenosis will not further complicate the picture A few people are very despondent over the use of a tracheotomy tube, and I know of one instance, in a case where a patient had bilateral abductor paralysis, who refused a tracheotomy tube and died of suffocation For those patients who are not willing to wear tubes, the operation of submucous resection is reserved It has been used in only eight cases in our Clinic, six of which have gotten excellent results

If the patient is a teacher or a saleslady, that is, if she depends on her voice for her living, then the wearing of a tube that has a valve in it, such as devised by Tucker (and there are other tubes on the market), permits them to talk very well, they can breathe well, and their only discomfort is the presence of a tube Many people are happy with such a tube, but when a person would rather die than wear one, it is justifiable to perform this operation, which does sacrifice the voice in large measure, but not entirely They at least have a hoarse whisper, very comparable to that of a person who has lost a vocal cord by its removal in carcinoma of the larynx

DR. FREDERICK A. COLLIER (Ann Arbor, Mich.) Injury to the recurrent laryngeal nerve has always been one of the feared complications of operations on the thyroid and yet it continues to be a very common occurrence—how common one never knows unless there is a routine examination of the larynx before and after the operation.

I have been greatly interested and instructed by Doctor Lahey's discussion of this subject both today and at other times. For years I, too, held to the doctrine I had been taught that elevation or dislocation of the lobes caused damage to the recurrent nerve, and every effort was made to avoid lifting the lobe until it was freed from the capsule and the thyroid tissue left behind. After an unfortunate experience while performing a total thyroidectomy, I adopted the method I saw practiced by Cutler, of exposing the nerves prior to removing the thyroid. This practice has gradually been extended until we use it frequently but not routinely in subtotal operations.

The recurrent laryngeal nerve, unlike the vagus from which it arises, is a relatively compact nerve with a thin epineurial sheath containing little fat. It is in contact with many unyielding structures and tolerates moderate trauma well. It is important to point out the marked differences in the courses of the right and left recurrent laryngeal nerves, as this has a real interest to those operating on the thyroid. The right recurrent nerve splits off the vagus behind the subclavian vein and turns backward and upward around the lower border of the subclavian artery and extends upward along the right border of the esophagus to terminate as the inferior laryngeal nerve. This inferior laryngeal nerve in its course upward is associated with the branches of the inferior thyroid artery sometimes lying between its branches, sometimes in front, sometimes behind them. In its course it extends along the lateral lobe of the thyroid and behind the cricopharyngeal muscle and behind the cricothyroid articulation, divides into a posterior ramus which supplies the cricoarytenoid posterior and the transverse arytenoid muscles—and an anterior ramus supplying the other laryngeal muscles with the exception of the cricothyroid which is supplied by the ramus externus of the superior laryngeal.

The recurrent nerve, on the left side, is given off at the arch of the aorta, it passes around the arch of the aorta and extends upward on the anterior surface of the esophagus to end as the inferior laryngeal nerve.

It can be seen that the differing courses of the right and left nerves offer dissimilar opportunities for injury. The nerve on the right side is shorter and since it lies closely in contact with the right lobe of the thyroid, can be easily injured during operative attacks on the gland, while the left nerve is comparatively protected by its position on the esophagus and is uncommonly injured.

A finding of paralysis of the left cord previous to operation would make one suspicious that the injury to the nerve occurred by a lesion in the thorax such as by aneurysm, mitral stenosis with enlarged heart, pulmonary infection or mediastinal tumor, while this finding on the right would presumptively be due to lesions high in the thorax or cervical region, perhaps a goiter. In our experience, preoperative injury to the nerve due to goiter is rare and when it occurs, not unusually is associated with carcinoma of the gland.

We hurriedly analyzed records of patients seen by Doctor Furstenberg in our Department of Otolaryngology over a period of several months and found 70 patients with paralysis of the cord or cords. Of these, 25 followed operations on the thyroid (in self-defense, may I say none came from our surgical clinic), two were associated with large goiters and two with carcinoma of the thyroid. Of the 25 injured nerves, 18 were on the right side, two on the

left and five were bilateral, demonstrating, I think, the relative chance of injury to the right and left nerves during operation

We have come to feel that elevation of the lobe, dissections around the lobe, formation of scar tissue following operation are relatively unimportant and infrequent causes of injury to the nerve. The nerve is usually injured by direct attack with hemostat, ligature or knife. We feel that an anatomic exposure of the gland and its surrounding structures tends to prevent nerve injury. This exposure should be especially imperative on the right side where injury is easy and more frequent. On the left side the operator really must go out of his way to injure the nerve.

We have tried very few nerve anastomoses without good results.

Doctor Furstenberg has used a modification of Hoover's operation in which the mucous membrane of the cords is held against the larynx after operation by the superimposition of a two-way, double arm tracheotomy tube. This has, in his hands, produced admirable results following operation for bilateral recurrent nerve palsy.

DR. EMIL GOETSCH (Brooklyn, N. Y.) I would like to say a word regarding injury to the recurrent laryngeal nerve in the treatment of the superior thyroid pole during thyroidectomy, as referred to by Doctor Lahey. We all know that such injuries do take place. It is a common practice, in delivery of the upper pole, to place the finger under the pole and then to elevate it against the tension of the superior thyroid artery. Considerable pressure is, therefore, required and it is during this maneuver that tension is exerted upon the recurrent nerve which lies very near and just medial and behind the pole. As you are aware, the superior thyroid artery divides into a posterior and an anterior branch. It is the anterior branch which is resistant and renders it difficult to elevate the pole. Accordingly, when the latter is large and thick, it is held down in the deep recesses of the neck. Accordingly, to avoid any possible tension upon the recurrent nerve, it has been my practice to free the pole in the following manner. An incision is made into the anterior leaflet of the suspensory ligament at the isthmus, which is then liberated from the trachea and divided. From this point, the avascular space between the larynx and upper pole is entered and the suspensory ligament is clamped, incised and followed upwards until one reaches the superior pole. Thereupon, the anterior branch of the superior thyroid artery as the latter divides at the pole is clamped and divided. This has released the tension holding down the pole, which can then be readily elevated without the necessity of placing the finger behind it. The pole is then resected together with the lobe, and a stump of thyroid gland is allowed to remain anterior to the posterior branch of the artery, which is accordingly spared. During such a procedure there is no tension whatever placed upon the tissues in the region of the pole, and the nerve as it enters the larynx at this level is not traumatized or stretched. By leaving a small stump of tissue adjacent to the posterior branch of the artery, there is a minimum of injury to the smaller vessels in this region and the consequent hemorrhage is practically nil. Deep clamping is therefore never necessary and the occasional injury to the nerve by clamps is also avoided. This method of procedure has been very helpful in the treatment of the upper pole.

I may say a word further on the possibility of injury to the recurrent nerve during or after the resection of large adenomatous goiters which have caused practically complete atrophy of an entire thyroid lobe, leaving a mere film of atrophic capsule between the goiter and the nerve. In the resection or enucleation of such goiters, I have found it advantageous to begin the

dissection of the lobe on the tracheal side, incising the capsule adjoining the trachea and by means of the finger between the goiter and the posterior capsule, rolling the goiter laterally instead of in the opposite direction. The capsule is thus readily recognized and spared and the possibility of injury to the nerve is, I believe, far less likely than in approaching the resection from the lateral side. Whatever tissue is present between the goiter and the nerve is thus kept intact and the occasional instance of hoarseness, four or five months after resection, is avoided.

If the resection is conducted from the lateral side, trauma in the region of the nerve is more likely, and I have felt that the nerve may occasionally be involved in a subsequent fibrosis with consequent functional injury. It is difficult to understand the reason for the late hoarseness on other grounds. Unfortunately, such hoarseness is apt to be relatively permanent as I have seen it in rare instances.

DR MONT R. REID (Cincinnati, Ohio) In my experience, I have been quite convinced that operating upon goiters with the head and the neck relaxed rather than hyperextended is definitely a safety procedure. By so doing, the gland can be lifted more readily out of the neck, while the nerve tends to drop backward out of the way. When one operates with the neck hyperextended, the muscles, the gland and nerve are taut, which makes it much harder to deliver the gland out of the neck and also increases the chance of injuring the taut nerve while working in a hole.

DR ELLIOTT C. CUTLER (Boston, Mass.) I would like to add a small anatomic experience to this excellent exposition by Doctor Lahey. During the experience of performing total thyroidectomy on more than 80 patients, we had to expose the recurrent nerves in every case in order to avoid injury to them. When I first attempted the operation of total thyroidectomy, I stood upon the right side of my patient, as had long been my custom in carrying out the operation of subtotal thyroidectomy. In the first 10 cases I twice injured the left recurrent nerve. From that time on I changed my position so as always to operate upon the thyroid lobe from the same side as the lobe, crossing from right to left when I had completed the right side and was ready to attack the left side. The result of this was that no further damage to the recurrent laryngeal nerves occurred.

Would Doctor Lahey, in closing, tell us whether he thinks it is desirable for surgeons performing subtotal thyroidectomies always to cross over when one side is completed, so that the operator will always be on the same side of the patient as is the lobe which is to be removed?

In this large experience with total thyroidectomies I have never found a recurrent nerve lying within the substance of the thyroid gland. This is a finding, of course, in agreement with the embryologic development of the gland and the nerve. They start as separate structures and must necessarily remain separate. I feel certain that the articles which have been published and which make the statement that the recurrent nerve passes into the thyroid gland through its posterior capsule are entirely erroneous and must be based on improper visualization of the structures. Of course, adenomata protruding from the posterior capsule may partially surround a recurrent nerve, but even in such cases the nerve never enters the posterior capsule.

Another matter which I have always thought important in thyroidectomy is the shift of position of the recurrent nerve when the gland is drawn forward sharply by traction. Under such circumstances the nerve, which invariably passes through branches of the inferior thyroid artery close to the

posterior capsule, is pulled forward with the gland. When this dislocation of the position occurs, a clamp hastily placed on the posterior capsule may include the nerve. Doctor Collier spoke of how some surgeons thought it unwise to dislocate the thyroid gland too greatly when removing it. This teaching, I think, emanates from the fact that when one does pull the gland forward, the dangers of catching the recurrent nerve in a hemostat are increased unless the surgeon is willing, as Doctor Lahey suggests, to visualize the nerve and separate the little vessel which is holding the nerve up. It is this same type of technical error that so often results in injury to the common duct. In this latter field, if the ampulla is stuck to the common duct and great traction is exerted, then the clamp, supposedly on the cystic duct, may also include a segment of the common duct.

This matter of the position and the visualization of the recurrent nerve is perhaps the most important knowledge for the thyroid surgeon if he is to avoid trouble. I cannot agree with Doctor Lahey that the nerve must be visualized in every instance, but I do agree that any surgeon who is performing operations upon the thyroid gland should make himself perfectly familiar with the usual position of the recurrent nerve by visualizing it, let us say, in somewhere between 50 to 100 cases.

DR EDWARD D. CHURCHILL (Boston, Mass.) The recurrent nerves are routinely visualized in operations for hyperparathyroidism, and I think it is fair to say that the nerves are exposed to more trauma and over a longer period of time than in any ordinary thyroidectomy. We have noticed no resulting injury to the recurrent nerves early or late, although a legacy of scar tissue must surround the nerve trunks. In one instance, I inadvertently cut one division of a bifid recurrent nerve and performed an immediate suture. For some reason it was never possible to detect any physiologic disturbance or change in function of the corresponding vocal cord.

An instructive situation was encountered in the case of an opera singer with carcinoma of the thyroid. Her larynx was examined a week before she entered the hospital and found to be normal. The morning after her arrival she said her voice had changed. There was a slight huskiness that I should not have detected but she was very much aware of it, being a singer. Laryngeal examination showed complete paralysis of the right cord.

I suppose that in a great majority of instances, paralysis of a recurrent nerve in association with carcinoma of the thyroid indicates malignant invasion. In this case, we proceeded with an emergency operation on the day that paralysis was first noted. The nerve was isolated and was not found invaded by malignant tissue, but definitely involved in the edematous reaction about a highly malignant tumor.

For her own mental comfort, her larynx was not examined until three months after this operation, when it was found that the right vocal cord moved normally.

The anatomic anomaly of the laryngeal nerve arising directly from the cervical vagus trunk I have encountered once. It is apt to be associated with an anomalous origin of the right common carotid directly from the arch of the aorta and passing transversely across the mediastinum behind the esophagus. This was confirmed by putting a finger down and feeling this anomalous vessel. It can be detected roentgenologically if you know enough to look for it before operation, as a notch in the esophagus is demonstrated by a swallow of barium.

DR FRANK H LAHEY (closing) In answer to Doctor Cutler's question, we have never performed a thyroidectomy without crossing to the opposite side of the table. How men can work upon thyroids standing on one side of the table and peering over to look in back in order to see the parathyroids, I have never been able to understand. I do not believe they do. The only way I think you can really see what is in back of the thyroid is to stand on the same side.

I purposely did not mention the question of cutting the prethyroid muscle because it usually causes such an acrimonious discussion. On the other hand, I feel very strongly that if this question of recurrent laryngeal paralysis does exist, and it does, if you can get better exposure by cutting the muscles, and you can, then you ought to cut the muscles. After all, they heal well, and we have cut thousands of them. It does no harm if you cut them high above their innervation.

As to lifting the lobe, I may not understand Doctor Cutler exactly, but I think we have not only lifted the lobe, we have hauled it up out of its bed and turned it upside down, and I do not think it makes one iota of difference. We have taught every surgeon who has been associated with the Clinic to palpate the recurrent nerve by pushing it against the trachea, as it has real body, and can be felt very definitely, even palpation of the nerve under tension does no harm.

Finally, anyone performing thyroid surgery should have a Berens' magnifying loupe. It will magnify two and one-half times, and the focal range is about 18 inches, so that one can keep away from the field and not run the danger of contaminating it. It is a very valuable means by which one can see the situations in nerves and distinguish them from vessels.

AMOUNT OF THYROID TISSUE TO BE LEFT IN OPERATIONS FOR DIFFUSE TOXIC GOITER

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IN 1912, William S. Halsted¹ wrote "Although thousands of operations have been performed, the world over, for the cure of Graves' disease, we are not yet in a position to state how much of the thyroid gland should be removed in any given case." It is still true today. This paper is based on a study of the relation of the estimated size of the gland remnants left at operation to the follow-up results.

It is known from the work of Halsted² and others that removal of a part of the thyroid in experimental animals is followed by compensatory hyperplasia in the remnant. According to DeQuervain³ investigation has shown that at least three-quarters of the gland may be removed without causing hypothyroidism, as long as the gland tissue is healthy. Halsted,¹ in one of his dogs, found that "Hypertrophy of hardly more than a film of transplanted gland plus, perhaps, the hypertrophy of minute accessory thyroids sufficed to cause the disappearance of myxedema."

In the human subject a very small fragment of normal thyroid may protect against myxedema. Berlin,⁴ in two patients with heart disease, removed approximately nine-tenths of the normal gland. The weight of the normal human gland is estimated at an average of 25 Gm., so that presumably 2 to 3 Gm. remained. There was a drop in metabolic rate and improvement in the cardiac condition, but during the fifth week the metabolic rate began to rise and improvement became less pronounced. Blumgart⁵ and his collaborators, in commenting upon the necessity of total thyroidectomy to relieve damaged hearts, say "It was not long before it was realized that anything short of complete removal of every vestige of thyroid gland would not permanently lower the basal metabolic rate."

In the early days of thyroid surgery, Kocher and Reverdin discovered the danger of complete extirpation of the gland from the standpoint of subsequent myxedema. It then became a common practice to remove one lobe only, but while many cases of Graves' disease were relieved by this limited procedure, the failures were too numerous and the extensive bilateral resection for toxic goiter gradually evolved with steady improvement in the results.

Thompson⁶ and his collaborators, in their study of postoperative hyperthyroidism at the Massachusetts General Hospital, found that the more experienced thyroid surgeons, who, they observed, did the most complete resections, had a lower incidence of persistent disease than those less practiced. Lahey and Clute⁷ state a commonly held belief that failure to return to normal is always due to too much hyperplastic tissue in the neck.

The difficulty of defining the proper amount of tissue to leave is illus-

trated by the fact that all surgeons recognize that it varies in different cases, and that many of the most authoritative writers do not go beyond general terms in discussing the matter. Crile⁸ leaves the smallest amount in the severest cases, those with very vascular glands and in originally small glands, but admits that the experience of the surgeon must be the final criterion. Lahey⁹ states that judgment depends on "the degree of involution in the gland, the age of the patient and the degree of improvement with iodine therapy during the period of preparation." He advocates "leaving in fairly good sized remnants in those patients whose glands have involuted well and doing very radical removal in those patients whose glands have not involuted well."

Brenizer¹⁰ leaves a wedge varying from one-quarter to one-half inch in width and thickness. McClure and McGraw¹¹ say that a mere strip of thyroid tissue should be left from the posterior aspect of each lobe. It is noteworthy that they report three times as many instances of postoperative hypothyroidism. Bartlett¹² and Hertzler¹³ advocate a similar procedure in adults. The latter does not fear postoperative myxedema.

Richter¹⁴ is among the most radical as well as the most specific in his description of the amount he leaves. In an article appearing in 1932, he stated that he had been reducing the remnant to less than 2 Gm but was inclined to leave more, possibly 2 or 3 Gm, because of the persistence of hypothyroidism in too many of his patients. He starts giving desiccated thyroid four weeks postoperative and continues as long as may be necessary, usually several months to a year or more. Most patients return to normal. Out of 447 patients examined after radical thyroidectomy, but one was found to be toxic.

Pemberton¹⁵ represents a more conservative school. He writes "One of the commonest errors into which many surgeons fall is the belief that recurrence of hyperthyroidism is always directly attributable to inadequate surgical treatment. This has led them to advocate and practice needlessly radical surgery, exacting, as it inevitably must, a higher toll of avoidable complications, such as injury to the laryngeal nerves and production of parathyroid tetany. Today these are far too excessive a price to be paid for the removal of goiter." The operation, as evolved at the Mayo Clinic, includes removal of the isthmus and resection of both lobes, leaving a remnant on each side equivalent to from one-sixth to two-thirds of the amount of tissue in a normal lobe. Expressed in grams this would represent two to eight on each side. As proof that very radical resection cannot guarantee against hyperthyroidism, he cites three cases of postoperative hypothyroidism, two of them definitely myxedematous, in whom exophthalmic goiter eventually recurred.

Ebberts¹⁶ leaves a mass on each side of the trachea equivalent in volume to one-third of a normal lobe, estimated roughly as the size of the terminal phalanx of the little finger. He is less radical where involution is advanced

Joll¹⁷ removes no less than seven-eighths of the gland, and in severe cases as much as nine-tenths, and ties all the main arteries

Estimation of Size of Thyroid Remnant—For a number of years the writer has been measuring the remnants after they were sutured over at operation by cutting out portions of corresponding size from the specimen removed and weighing them, thus arriving at an estimate of the amount of gland tissue left in the neck. Seventy-five patients with diffuse toxic goiter in whom this procedure has been carried out and who have been followed with metabolism tests for from eight months to six years form the basis of this study. Three of the patients had had a previous resection. Cases of nodular toxic goiter have not been included because it is felt that the diffuse type, in which the tissue changes are of a uniform nature, lend themselves better to a study of this kind.

No one who has attempted to determine the amount of thyroid tissue left at operation is more aware than the writer of the inaccuracies of the method. The weighing has been done after the operation has been concluded, which means that the specimens may have lost in the interval from drying. As a check two observations were made. In the one case a small specimen was weighed in the operating room and again after the operation without notable change. A second specimen which weighed 76 Gm immediately after removal was found to be 68.5 Gm on standing until after the operation was completed. This, however, is not a serious source of error, as the proportion of the remnants to the size of the gland is small. More important is the fact that the remnants are irregular in shape, and while they are measured in three planes, one is aware that the blocks cut out from the specimen are at best a rough approximation. Finally, there may be extensions of the remnant which the operator fails to appreciate. Nonetheless, with all the objections, the method offers a more concrete basis for judgment than visual or tactual appraisals alone.

There have been no deaths during the period of this study which would allow of securing at autopsy and weighing the actual remnant as a check on the estimate. The writer has, however, carried out the procedure in the autopsy room. Such observations indicate that small to medium remnants have probably been underestimated by about 2 Gm.

Of the 75 patients studied, ten, or 13 per cent, showed postoperative hyperthyroidism. Another has had a basal metabolic rate that is often somewhat above normal but as she has had no symptoms she is not considered recurrent. Of the ten cases, eight are continuations. Of the two remaining, one was definitely hyperthyroid at the end of a year and the other, two years. Metabolism tests obtained in the interim on the first were +11 and +15 per cent, on the second, +27 per cent, so that these patients may not have been completely relieved of their toxicity at any time.

The estimated size of the remnants has ranged between 3 and 25 Gm. Thirty-seven were recorded as 6 Gm or less and 38 as 7 Gm or more. If 2

Gm are added as a correction, the division would come between 8 and 9 Gm instead of between 6 and 7—probably closer to the actual amounts

The proportional size of the remnant was calculated by adding its corrected weight (estimated weight plus 2 Gm) to that of the specimen, and dividing the result, the weight of the whole gland, by that of the corrected remnant. Forty were found in this way to have one-seventh, or less, of their gland remaining, and 35 one-sixth or more, the proportions ranging from one-twentieth to one-third.

Factors Other Than Size of Remnant Influencing Result of Treatment—

If all cases in the series were identical the study of the effect of the different sizes of remnant on the outcome of the operation would be much simplified. Of the variables which have to be considered, that of primary importance is the severity of the disease. In order to take account of this factor the series has been divided into two, on the basis of elevation of basal metabolism before treatment. As would be expected, the great majority of patients with postoperative hyperthyroidism came from those in the higher range, eight as opposed to two in the lower range. Size of the gland is a factor of at least technical importance. There were more large glands among the severer cases.

Involution has been mentioned as a factor in judging the amount of gland tissue to leave. In this series the writer has not recognized any notable trend on the basis of iodine response. Those in whom the metabolism fell to below +20 per cent, on their preoperative iodine, had a very low incidence of postoperative hyperthyroidism. They were, however, almost altogether drawn from the milder cases.

Three patients of the series were adolescents, age 13 and 14, too few to furnish any conclusions as to treatment in the young. In general, however, the writer prefers to be conservative in resections in this age-group. The oldest patient was age 60.

It is now proposed to examine the effect of the size of the remnant considered from the two aspects of weight and proportion on (1) The general metabolic outcome of the series, (2) the incidence of postoperative hyperthyroidism, (3) the incidence of postoperative hypothyroidism, and (4) individual cases.

*Size of Remnant and Metabolic Result—*A composite metabolism progress chart has been prepared of the two groups of the series based upon the weight of the remnants. Persistent and recurrent cases are included until such time as they may have been submitted to roentgenotherapy or reoperation (Table I).

It is seen from analyzing Table I that there is no apparent difference in the collective outcome, although the group with lesser remnants contains a larger proportion of milder cases, as is also evidenced by the lower average of first metabolism tests.

A similar chart has been prepared based upon the proportion of the remnants, with the correction of 2 Gm added, to the size of the gland (Table II).

In the division, as seen in Table II, the group with proportionally smaller

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remnants contains a much larger proportion of the severer cases, which is reflected in the higher average admission metabolism. There is nothing to choose in the collective aftercourse.

TABLE I
COMPOSITE METABOLIC RATE

	Six Gm or Less		Seven Gm or More	
	Corrected, 8 Gm or Less		Corrected, 9 Gm or More	
	B M R	No of Cases	B M R	No of Cases
Admission	+51	37	+62	37
Preoperative	+23	37	+28	38
Postoperative	+ 1	35	+ 2	34
3 months	+ 6	21	+ 4	24
6 months	\pm 0	26	\pm 0	28
1 year	\pm 0	28	\pm 0	33
2 years	\pm 0	24	+ 2	22
3 years	- 5	15	+ 2	14
4 years	+ 5	9	- 2	13
5 years +	- 4	9	- 3	10

TABLE II
COMPOSITE METABOLIC RATE

	Remnant			
	One-Seventh or Less		One-Sixth or More	
	B M R	No of Cases	B M R	No of Cases
Admission	+65	40	+46	34
Preoperative	+30	40	+20	35
Postoperative	+ 3	37	+ 1	32
3 months	+ 5	26	+ 6	19
6 months	+ 1	32	- 1	21
1 year	- 1	34	+ 1	27
2 years	+ 2	24	- 2	20
3 years	- 3	18	- 1	10
4 years	+ 2	13	- 2	7
5 years +	- 4	9	+ 1	9

In order to approach the question from a somewhat different aspect, the series has been divided into three groups: (1) Those whose postoperative basal metabolism tests have averaged less than ± 0 , 35 in number, (2) those who have averaged above ± 0 but have not been considered hyperthyroid postoperatively, 30 in number, and (3) the ten with persistent and recurrent hyperthyroidism.

As between groups (1) and (2), the former contains a larger proportion of mild cases. The average size of remnants is the same. Group (3), made up of the ten persistent and recurrent cases, contains a preponderance of originally more toxic patients, while the size of the remnants averages 10.5 Gm as opposed to 7 in the remainder of the series.

Size of Remnant and Incidence of Postoperative Hyperthyroidism—Approaching the subject now from this aspect, one finds that in the half of the series with smaller remnants by weight the incidence of postoperative hyperthyroidism is 8 per cent as opposed to 18 per cent in those with larger rem-

nants The former group, however, contains 62 per cent of milder cases which modifies the significance of the figures Dividing the series into thirds, that with smallest remnants has fewest failures

Where the series is divided into two, on the basis of corrected proportional size of the remnants, there are an equal number of persistent and recurrent cases in each group The result must be considered better, however, in the group with smaller proportional remnants, as it contains 70 per cent of severer cases Dividing the series into three, the third with smallest remnants proportionately includes only one patient with persistent hyperthyroidism, although it is made up largely from the severer cases

Among the ten failures in the series studied, seven had remnants above the median in weight and three below Of these three below, all were from relatively small glands and fell among those with the largest remnants proportionately It would seem that a reduction in thyroid tissue that was thorough, both from the point of view of actual as well as proportional size, should be followed by a minimum of postoperative hyperthyroidism

Size of Remnants and Postoperative Hypothyroidism—There are six patients who have been given thyroid medication for a period but none have had to remain on it permanently These six include both severer and milder cases as well as those with smaller and larger remnants It is apparent, however, that postoperative hypothyroidism may ensue despite a good sized remnant of thyroid tissue

Size of Remnant in Individual Cases—When the persistent and recurrent cases are reviewed individually one feels, in almost all instances, that had the resection been more radical the result would have been better

ILLUSTRATIVE CASES

Case 1—Mrs C, age 27, married had a primary basal metabolism rate of +55 per cent Seventy-nine grams of thyroid tissue were removed The remnant was estimated to be 12 Gm, considerably above the average of the series Three months after operation the metabolic rate was +41 per cent, and she was not well She had roentgenotherapy and responded promptly Since then her tests have been within normal limits, the last one -6 per cent, nearly six years after operation

Case 2—Mrs P, age 48, was hypertensive as well as hyperthyroid, and presented a different aspect of the problem Her primary metabolism rate was +71 per cent The gland was a small one, the specimen weighing 17 Gms and the remnant being estimated at 6 On the seventh postoperative day the metabolism was +5 per cent, but by the end of four months it had risen as high as +36 per cent She received roentgenotherapy, which completed the cure as far as we have been able to observe her In this instance the remnant was small by weight but large in proportion to her original supply of gland tissue

However, what seems like an adequate resection will not always insure a satisfactory result

Case 3—Miss R, age 30, had a primary metabolism rate of +50 per cent, and a second of +41 per cent before treatment The specimen weighed 28 Gm and the remnant was estimated at 5 Although the patient gained 20 pounds and looked well, she had a metabolism rate at nine months of +20 per cent and at 11 months of +28 per

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cent, accompanied by symptoms of fatigue and emotional instability. On iodine her metabolism rate has remained within normal limits during the past few months but she still has symptoms.

In this instance the remnant was small, and while its proportion to the size of the gland was greater than the median of the series, the operator felt that he had, if anything, gone too far, as the toxicity was not severe and the gland of normal size.

Case 4—Mrs. S., age 37, shows that the patient may do well as could be wished despite the fact that she has been left with considerable thyroid tissue. On admission her basal metabolism rate was +64 per cent. At operation the estimated remnant was large by weight, 11 Gm, and also proportionately to the size of the goiter. Postoperative metabolism tests have been at six months, +1 per cent, at one year, -9 per cent, and at four years, -13 per cent.

Case 5—Mrs. P., the only one of the series to come to reoperation thus far, is presented to illustrate regeneration. At the first operation the specimen weighed 74 Gm and the remnant was estimated at 9. At the second operation, two years later, 19 Gm were removed, leaving an amount estimated at 5 Gm.

SUMMARY AND CONCLUSIONS

The power of regeneration of the thyroid gland is very great. The accumulated experience of surgeons has been that resections for toxic goiter must be extensive in order to keep the incidence of unsatisfactory results at a low figure, although many successes have been recorded after what is now considered inadequate surgery.

In the series under review the writer has attempted to perform thorough but not extremely radical resections. The record of 13 per cent relapses, a figure which may well be increased after a longer period of observation, in some of the more recent cases particularly, would argue that, in general, criticism might point rather toward too great conservatism than otherwise.

One cannot place too much confidence on statistics based upon such rough methods of estimation as have necessarily been employed, yet it is felt that they have some value.

The most important factor in planning the extent of operation is the severity of the disease. Size of the gland, both for its bearing on technical difficulties as well as on the relative proportion of remnants to be left, is also important.

Studies on the collective outcome of the series would seem to indicate that, within the limits of resections performed, there was not much to choose between larger and smaller remnants. When, however, the incidence of persistent and recurrent cases is used as a criterion, the results favored the smaller remnants both on the basis of actual weight and relative proportion. Examination of the individual failures showed that in no case did the remnant fall into the smaller half of the series on both counts. This indicates that not only must the operator plan on leaving a small remnant but that he must be guided in his judgment by the size of the original goiter and in the case of small very toxic glands be particularly radical. This is only logical when

one recalls that an equally severe grade of intoxication may be found in the presence of glands of very different sizes

On the basis of this study, the writer thinks that a remnant of 4 or 5 Gm as he has estimated it, or as corrected, 6 or 7 Gm, should result in fewer failures. To present the matter more concretely, blocks of tissue measuring 3x1x1 cm from two specimens of hyperplastic iodized glands were weighed and found to be 2 to 2½ Gm. This amount on each side of the trachea seems a satisfactory amount to allow to remain in the more toxic cases unless the gland is small. In the case of medium to good sized glands, a remnant of 5 Gm would represent a small proportion of the original goiter, say one-tenth or less, a relative amount which in the series studied was followed by a low incidence of postoperative hyperthyroidism. In the case of glands which are little larger than normal, despite a marked toxicity, one should leave smaller amounts than usual so that the relative reduction of thyroid tissue is thorough. In large glands with only mild toxicity, on the other hand, more generous remnants ought to meet the indications.

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DISCUSSION—DR WILLIAM BARCLAY PARSONS (New York) Doctor Smith's interesting paper brings up certain points of technical and philosophic importance that are worthy of comment. In my opinion, it is doubtful if we are entitled to assume that the behavior of the gland remnant left behind after operation on a pathologic gland will be similar to that of normal thyroid left by mistake in attempting total thyroidectomy for heart disease. The former would be far more subject to either regressive or progressive change, while the latter would have a tendency toward normal behavior.

One naturally agrees with all the general principles laid down by Doctor Smith. One cannot help having some doubt as to the estimation of the weight of the remnant, particularly if one has had experience in the technic. In 1930 and 1931, Gutman, at the Presbyterian Hospital in New York, was interested in estimating the total weights of thyroids in the course of some iodine studies he was pursuing. We estimated the gland remnant for him by measuring the remnant before suturing, which should be accompanied by less error than after suturing. To indicate roughly how much a fresh piece of thyroid weighs, one flat pear-shaped piece measuring $1\frac{1}{8}'' \times 7\frac{7}{8}'' \times \frac{1}{4}''$ weighed 6 Gm, another measuring $1'' \times 7\frac{7}{8}'' \times \frac{1}{8}-\frac{1}{4}''$ weighed 4.5 Gm. Pieces of this size are by no means large, but were adequate for these two particular cases, as they were in satisfactory condition when last seen, six and seven years after operation. We really had but little confidence that our measurements came within an error of 10 per cent, and it is probable that we all leave far more tissue behind than we believe we do. Fortunately in the vast majority of cases a balance is reestablished—the same kind of accommodation that follows other surgical procedures involving the sacrifice of part or all of an important organ or viscus.

As Doctor Smith points out, we should make an attempt to fit the operation to the case according to the suggestions in his paper. The greatest difficulty is in the cases with very small, highly active glands. In these, one is forced to leave a relatively tiny remnant and one runs the risk of serious impairment of blood supply to this small piece.

In all cases, as individual problems, there is the decision to be made, if one has to miss the ideal, whether one wishes to err on the side of too conservative or too radical a removal of tissue. Here is where one's philosophic point of view affects one's technical procedure. As a rule the conservative appeals to me. A few cases of persistent hyperthyroidism are far easier to handle than a few cases of persistent hypothyroidism. Radiotherapy will straighten out three-quarters of the former, the balance requiring reoperation. In my experience hypothyroidism has usually been permanent, and these individuals have, I firmly believe, a greater quality and quantity of unhappiness than those with persistent hyperthyroidism. People with hypothyroidism are uncomfortable and unhappy. Thyroid extract will of course help to a degree, but it is at best a poor substitute for an adequate supply of one's own thyroid secretion. It is also a misfortune when one has to live with a bottle of pills, from both financial and psychologic reasons.

DR EMIL GOETSCH (Brooklyn, N. Y.) I would like to say a few words with reference to the remnant remaining after thyroidectomy which Doctor Smith has discussed in detail. In the hyperplastic thyroid gland that has been untreated medically with iodine, there follows, after the intensive preoperative

treatment with iodine, a marked accumulation of colloid, in other words, a marked involution together with a good clinical remission. However, in those instances of hyperplastic thyroid glands which have been treated medically with iodine, perhaps for weeks or months, the preoperative intensive treatment with iodine is not followed by satisfactory involution or by a good clinical remission. Accordingly, one should leave a larger remnant in the case of the colloid gland with a good involution than in the latter instance.

I think it is of the greatest importance to visualize the histologic appearance of the gland that we are resecting, for when we are considering remnants purely in respect to their weights, we may be talking about the weight of the contained colloid that we are leaving behind, which has little to do with the future outcome of the operation. In the remnant, we naturally are planning to leave a certain amount of thyroid parenchyma and if one visualizes the relative amount of parenchyma which one is leaving in the remnant, then I believe we are on a correct basis as to the amount of real thyroid gland which we are leaving for future functional purposes. I believe it is a safe practice to resect the thyroid gland more radically in instances of extreme toxicity in which there is the highest degree of hyperplasia. In other words, the more hyperplastic the gland, the more radically I believe one should proceed. The possibility of recurrence is thus minimized. Recently I saw an instance of recurrence of hyperthyroidism in a woman upon whom I had operated eight years previously, having performed a double resection for exophthalmic goiter. In a review of the history, I found that this woman had an unusually large and extremely vascular gland which was strikingly hyperplastic and of a somewhat beefy, meaty appearance. Following the operation, she developed extremely critical postoperative reaction which was as severe as I had ever seen other than in fatal cases. She fortunately recovered. It would seem that the intense potentiality of developing exophthalmic goiter was not entirely eliminated by the thyroidectomy and that this potentiality was sufficiently strong to develop recurrent hyperthyroidism after eight years.

A further word with reference to the thyroid remnant. Some years ago, during my association with Doctor Halsted, I had occasion to observe the results after single lobectomies, and was surprised to see a rather large number of patients who recovered satisfactorily and apparently remained well following a single lobectomy. In my own earlier experience, before the preoperative use of iodine, I too had performed a considerable number of single lobectomies for exophthalmic goiter in young girls whose further course I was able to observe. Many of these patients subsequently married, had children and remained well over a considerable period of years. These facts indicate that in our concern regarding the size of the remnant to be left behind after thyroid resection, we are considering only one element in the recovery from the very complex disease of exophthalmic goiter. There are many factors concerned other than the size of the remnant and if nature were not on our side as surgeons, we would have a difficult time in the treatment of this disease.

I should like to say a word on one further point and that is with reference to the status of the hyperthyroid patient in the early weeks after thyroidectomy. It is of course dramatic to note a normal metabolic rate and a disappearance of practically all symptoms in the early weeks after thyroidectomy. Such prompt return to normal is often destined to be followed by a late hypothyroidism, two to three or four years or longer, after thyroid resection. In other words, the resection has been too radical and the remnants of thyroid gland remaining after resection too small. In other words, I prefer to leave somewhat larger remnants and see the return to normal following operation occur more gradu-

ally over a period of two to three months, for these patients are destined to remain well and to be more nearly normal than patients who present more normal findings within a few weeks after operation

DR MARTIN B TINKER (Ithaca, N Y) Doctor Smith spoke of the weight of the gland, mentioning the size of the fragment left with relation to weight His experience checks well with our own As a rule you cannot reduce the size of the fragment remaining to less than 3x1x1 cm, and get satisfactory thyroid secretion On the other hand, there are, as Doctor Smith has said, cases in which it is necessary, because of low activity, to leave a larger fragment One of the best ways to arrive at a decision as to how much to leave is to have all interested study the gross specimens in comparison with the microscopic and clinical findings Any man who will go over 500 specimens in that way, better still 1,000, will get a good idea from the gross appearance of the gland in the neck and the gland when cut, as to how much it is necessary to leave behind In over 7,000 cases, we have had less than 1 per cent of hypothyroids, also less than 1 per cent, during recent years, of operations for recurrence

The function of the thyroid depends upon its circulation, and it seems unwise to cut off too much blood supply We do not ligate the inferior thyroid artery If radio cutting is used, hemorrhage is controlled without trouble or injury to the artery, and by dividing well up onto the capsule, it is possible to safeguard the parathyroids and enough circulation so that the fragment left will function well and take care of the needs of the patient

It is very true that in certain instances, a large fragment can be left with satisfactory function Doctor Schweitzer will remember the cases that Dr Theodor Kocher operated upon with serious resultant myxedema, where he removed only one lobe, and in my earlier cases, I followed Kocher's technic Some patients have remained well for 30 years and over, where a single lobe was removed However, that would not apply to the diffuse goiters that Doctor Smith is talking about They must have the gland reduced decidedly, best judged after careful study of the gross and microscopic appearance has taught how much to leave and also by maintaining adequate circulation of the stump of gland left

THE IODINE METABOLISM IN EXOPHTHALMIC GOITER*

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IODINE and thyroid function are inseparably related. The thyroid gland is a principal storehouse for iodine. The thyroid hormone has a high iodine content. The utilization of iodine to form thyroid hormone is thus an integral part of thyroid activity. As a consequence the metabolism of iodine becomes of fundamental significance in the investigation of thyroid physiology, and of the changes in function incident to the development of thyroid disease. The use of iodine in the prevention of goiter has long been known. Since the contributions of Plummer, its use in the preoperative management of exophthalmic goiter has become common clinical knowledge.

Nevertheless, during the past decade newer facts have been added to the iodine story. It is established that iodine is constantly present in human blood. In what form it circulates is not yet clear, although presumably a part, at least, actually exists as thyroid hormone. There is a variable daily loss of iodine in the urine, feces and sweat. The level of the blood iodine fluctuates, likewise the daily excretion in the urine. These findings have gradually assumed clinical significance.

During the past eight years a group of us, including Davis, Cole, Phillips, Barron and Matthews, have investigated various phases of iodine metabolism in over 200 patients with exophthalmic goiter. For determining the minute amounts of iodine present in the blood and urine we have employed three methods. First, an adaptation of the von Fellenberg procedure which was developed by Davis¹. Second, a similar basic ashing method which was further refined by Phillips². Third, our present method is a closed, chromic acid oxidation procedure derived by Matthews³ from the Leipert principles, which yields lower values for the blood iodine.

It is difficult to adequately condense the available material. However, further details, together with other tables and charts, are available in current publications^{4, 5, 6, 7}. In the present communication we wish to present four features of the metabolism of iodine in exophthalmic goiter. These concern (1) the iodine content of the goitrous thyroid gland, which is decreased, (2) the blood iodine, which is usually increased, (3) the urinary excretion of iodine, which is usually increased, and (4) the iodine balance, which reveals a depletion of the patient's usual reserve store of iodine.

In order better to understand the pathologic iodine metabolism which exophthalmic goiter presents, it is clarifying to consider its two principal features. Our studies⁶ have clearly demonstrated a greatly increased mobilization of iodine with a subsequent depletion. This is comparable to the increased

* This work was aided by a grant from the Committee on Scientific Research of The American Medical Association.

mobilization of calcium and the ensuing calcium depletion which occurs in hyperparathyroidism

THE THYROID GLAND IODINE—*The Thyroid Gland Iodine Is Decreased in Untreated Exophthalmic Goiter* The normal iodine content of the human thyroid gland varies from 8 to 10 mg. The wet weight concentration varies around 40 mg per cent, while the dry weight concentration ranges around 200 mg per cent. It is significant that this iodine is contained principally in the colloid substance. Variations occur, physiologically, seasonally and geographically. Thus, the iodine content is lower during the winter months, and higher in persons living in coastal cities where the iodine intake is greater.

Since the original contributions of Baumann it has been known that the diffuse hyperplastic gland, characteristic of exophthalmic goiter, has a diminished iodine content. This observation has been repeatedly confirmed, and more recently by Lunde. It signifies iodine loss and is directly correlated with the loss of colloid substance from the more cellular, hyperplastic alveoli.

Thyroid iodine depletion may also ensue during the course of severe infectious diseases. It may be produced experimentally by the administration of the thyreolytic hormone.

THE BLOOD IODINE—*The Blood Iodine Is Usually Increased in Untreated Exophthalmic Goiter* Extensive clinical investigation, subsequent to the studies of Veil and Sturm, has established the value of the blood iodine as a measure of thyroid function. It is usually increased in patients presenting hyperthyroidism, and decreased in those with hypothyroidism. It has become a clinical aid in recognizing hyperthyroidism. In those unusual instances where it is not increased, it has been shown to have prognostic value. Its clinical significance has consequently become similar to that of the blood sugar in recognizing functional variations of the islets of Langerhans, or of the blood calcium in determining changes in parathyroid activity.

TABLE I
IODINE METABOLISM IN EXOPHTHALMIC GOITER

Case No	Sex	Age	B M R	Blood Iodine Micrograms %	Urinary Iodine Micrograms Daily	Days Observed
332556	F	17	Plus 18	30.9	169	8
331377	F	18	Plus 47	21.2	65	13
326974	F	32	Plus 32	29.1	106	5
326035	M	34	Plus 75	26.7	196	2
332609	F	35	Plus 95	13.5	159	7
326431	F	35	Plus 50	35.0	111	2
331567	M	38	Plus 50	22.7	105	7
335185	M	39	Plus 44	18.0	146	4
335167	M	48	Plus 53	20.8	310	3
335262	F	51	Plus 109	27.5	133	1
335262	F	51	Plus 93	30.6	230	3
Averages			Plus 69	26.0	157	5
Normal Averages			Plus 10	12.0	51	18
			Minus			

The majority of patients with untreated exophthalmic goiter present an increased blood iodine (Tables I and II). Results obtained from the earlier methods of analysis yielded higher values for the blood iodine than are now found (Table I). These older methods, however, revealed that the blood iodine averaged more than twice normal in patients with exophthalmic goiter. Newer methods reveal a lower normal blood iodine (Table II). Nevertheless, they also show that it is increased to more than twice normal in exophthalmic goiter. The proportional increase in exophthalmic goiter is similar by either method.

TABLE II

THE IODINE BALANCE IN EXOPHTHALMIC GOITER

As Compared with Normal Individuals and Patients with Nodular Goiter

Type of Goiter	Number of Patients	Total days of Investigation	Average B M R %	Average Blood Iodine Mcg * %	Average Daily Output				Average Daily Intake Mcg	Average Daily Balance Mcg
					Urine Mcg	Feces Mcg	Sweat Mcg	Total Mcg		
1 None normal persons	3	24	Minus 7	4.3	51	11	9	71	29	-42
2 Nontoxic nodular	2	18	Minus 8	3.0	40	10	10	60	25	-35
3 Toxic nodular	2	15	Plus 28	8.5	107	50	13	170	39	-131
4 Exophthalmic	3	33	Plus 40	9.0	68	55	15	138	29	-109

* Mcg denotes a microgram (0.001 mg.)

The nature of this increased blood iodine is not clear. It appears to be principally in the alcohol insoluble fraction, which has been designated "organic." Presumably it represents a greater circulation of the high iodine-containing thyroid hormone or of its metabolic products.

There is no direct parallelism between the blood iodine, the urinary excretion of iodine and the basal metabolic rate in patients with exophthalmic goiter (Table I). As a rule, however, all three are increased. Each of the three, however, dependent upon the phase of the disease, may lie within the normal range. Thus, in a late stage of untreated exophthalmic goiter we would ordinarily expect a resultant pronounced iodine depletion to have occurred. This should have an effect upon the blood and urinary iodine.

Iodine tolerance tests have been applied to the diagnosis of exophthalmic goiter. These depend upon the rate at which the injected iodine is removed from the blood stream, as shown by subsequent blood iodine determinations. The progressive iodine depletion of exophthalmic goiter is a significant factor in the evaluation of these procedures. The depleted tissues and particularly the depleted thyroid gland appear to remove more rapidly the increased circulating iodine.

The prognostic value of a low blood iodine in patients with exophthalmic goiter is brought out by the studies of Perkin and Hurxthal.⁸ It has been our experience that the increased blood iodine usually found in exophthalmic goiter returns to a normal range subsequent to an adequate thyroidectomy. They have shown in addition that these patients present no evidence of recurrence. On the other hand, in those patients with a normal blood iodine pre-

operatively, they even find a postoperative increase, and point out an increased tendency to recurrence

THE URINARY EXCRETION OF IODINE—*The Urinary Excretion of Iodine Is Usually Increased in Exophthalmic Goiter*⁵ Iodine is a normal constituent in human urine. The daily excretion fluctuates, however, and appears to depend principally upon the variable food intake, which is inconstant. When a constant, monotonous food regimen is maintained, the daily urinary loss is more uniform.⁹ The age of the individual appears to be a factor. Variable physiologic states, such as menstruation, have a demonstrable effect. The amount of iodine excreted in the urine varies geographically.¹⁰ It is low in those regions where goiter is endemic, as in central Ohio, where it averages 51 micrograms daily. It is increased in localities which are relatively goiter-free, as in New Orleans, where it averages 117 micrograms daily. These latter observations have a definite bearing upon iodine deficiency as related to the incidence of goiter.

The majority of patients with exophthalmic goiter reveal an increased loss of iodine in the urine (Table I). Thus 13 normal persons excreted from 36 to 78 micrograms daily, and averaged 51.¹⁰ In contrast, 24 patients with exophthalmic goiter lost from 46 to 357 micrograms daily in the urine, and averaged 147, which is approximately three times greater than normal.⁵

It is suspected that this increased urinary loss of iodine originates in an increased breakdown of the high iodine-containing thyroid hormone. However, this may not prove to be the only factor since other tissue iodine may play a part. To be correlated with this are the increased blood iodine and the loss of iodine from the hyperplastic thyroid.

The precise form in which iodine is excreted in the urine has not been determined.¹¹ It does not appear to be in the form of thyroxin, either chemically or biologically, but rather in a more simple compound. Solution of this particular problem is important.

We have elsewhere presented extensive data of the urinary excretion of iodine of normal individuals,¹⁰ of patients with exophthalmic goiter,⁵ and of patients with other thyroid diseases.⁹ From these studies it appears that the urinary iodine is of similar significance in disturbances of thyroid function as is the urinary calcium in parathyroid disease.

Nevertheless, in extending these studies it soon became apparent that the blood or urinary iodine represented but fractions of the entire process of iodine metabolism. The blood iodine normally less than 1 mg, presented the amount in circulation, although a part of this presumably existed as thyroid hormone or its iodine-containing split products. Another part presumably represented the iodine of nutrition.

Moreover, determinations of the urinary iodine did not present sufficient evidence concerning the intake, utilization or storage of iodine. Therefore, it became increasingly evident that the *iodine balance* should be determined. This meant the institution of carefully controlled hospital conditions for measuring the intake of iodine in the food, water and air, as well as its excretion.

in the urine, feces, sweat and expired air. The difference between the determined amount of intake and output would then yield a *balance*. In case storage were occurring, this would be positive. With an excretory loss greater than the intake, it would be negative.

THE IODINE BALANCE—*Exophthalmic Goiter Presents an Increased Negative Iodine Balance*⁶ It is of advantage to understand something of the normal variables and fluctuations of the iodine balance, in normal individuals as well as in patients with nontoxic goiter, before reviewing the abnormality presented by exophthalmic goiter. Detailed studies of these basic considerations are presented elsewhere^{6, 7, 12}

Normal persons maintained on a low iodine intake reveal a low negative iodine balance (Figs. 1 and 2, Table II). They appear to require a certain amount of intake iodine daily to remain in balance. Thus three normal individuals with a decreased intake of 29 micrograms of iodine daily excreted 71, resulting in a daily negative balance of 42 micrograms. Fifty-one micrograms, or 72 per cent of the iodine, was lost in the urine. Eleven micrograms, or 15 per cent, was excreted in the feces, while nine micrograms daily, or 13 per cent, was lost in the sweat (Table II).

It is possible to increase the intake iodine by adding to the diet milk with an increased iodine content. This has been prepared by giving dairy herds feeds containing supplemental iodine¹³. When maintained on such a diet, containing adequate iodine, normal persons remain in positive balance, and may even store considerable amounts of iodine (Chart 1). Too, this storage may be increased by the addition of potassium iodide to their diet (Chart 1).

During a period of starvation the negative balance is not only maintained, but may even increase somewhat (Chart 2). This further indicates a constant daily requirement of iodine, a part of which is presumably to be used in the formation of the high iodine-containing thyroid hormone.

The iodine balance of patients with nontoxic nodular goiter resembles that of normal persons, with possibly an even greater tendency to storage⁷. It is quite dissimilar to that of exophthalmic goiter patients, since the increased mobilization of iodine is lacking, as well as the subsequent depletion (Table II).

Two patients with nontoxic nodular goiter, maintained on a low iodine intake over a total period of 18 days, showed an average negative iodine balance which was within physiologic limits (Table II). The intake iodine averaged 25 micrograms daily while the output averaged 60 micrograms, resulting in a daily negative balance of 35 micrograms. The greatest excretion was in the urine, averaging 67 per cent. Seventeen per cent was excreted in the feces and 16 per cent was lost in the sweat.

One patient (Chart 3) even showed a greater retention of iodine than normal persons similarly controlled (Table II). This tendency of patients with nontoxic nodular goiter to store iodine, rather than to excrete it, has been noted by Scheffer and v. Megay¹⁴.

Elsewhere, we have presented extensive data which reveal the great dis-

turbance of iodine metabolism found in exophthalmic goiter ⁶ The increased mobilization of iodine is shown in the rise of the blood iodine, and by the

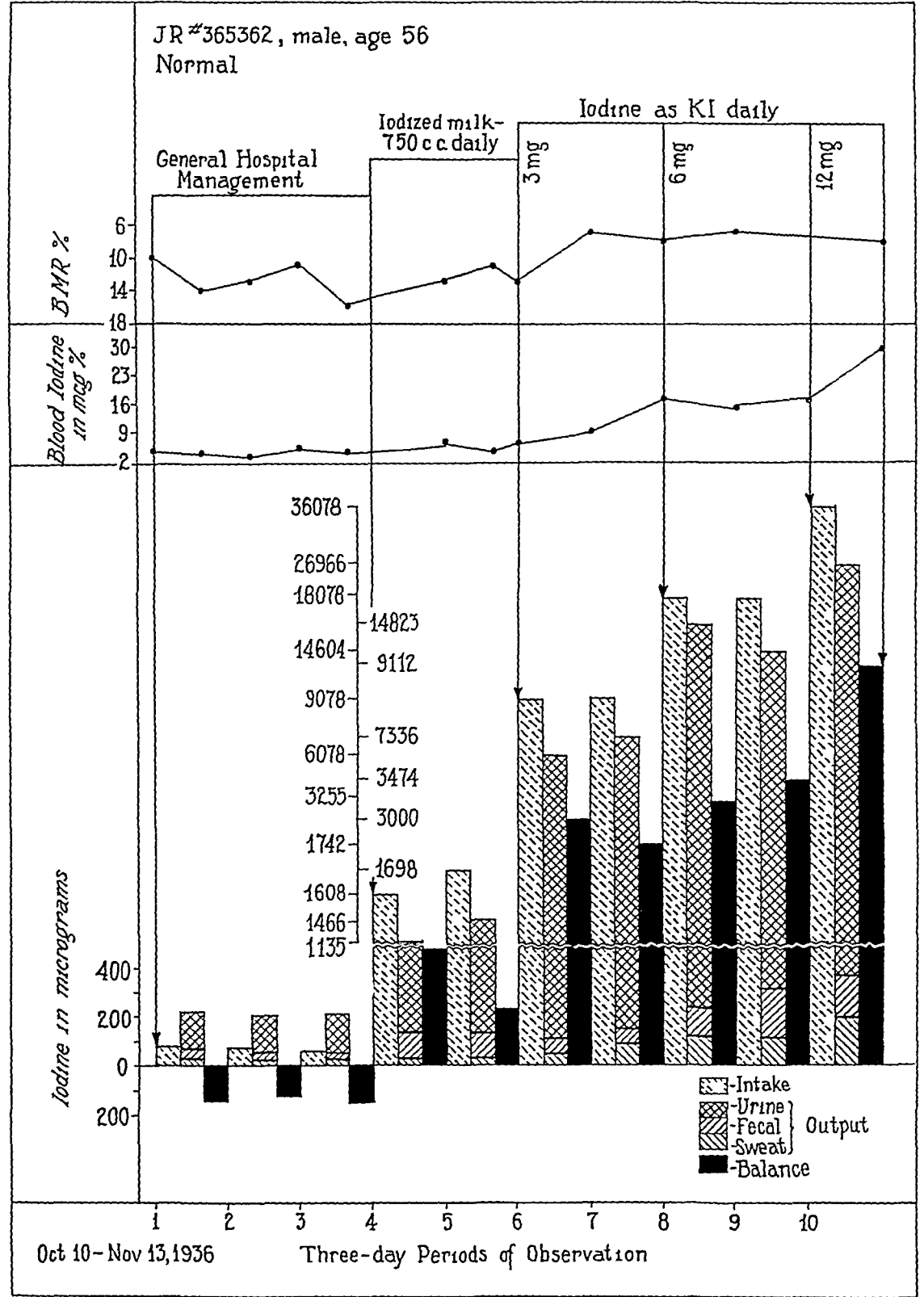


CHART 1—The iodine balance in a normal individual. Note the negative iodine balance on a low iodine intake and the effect of increasing the intake.

greater excretion of iodine in the urine, feces and sweat. Moreover, subsequent to this increased mobilization, iodine depletion ensues. This is revealed

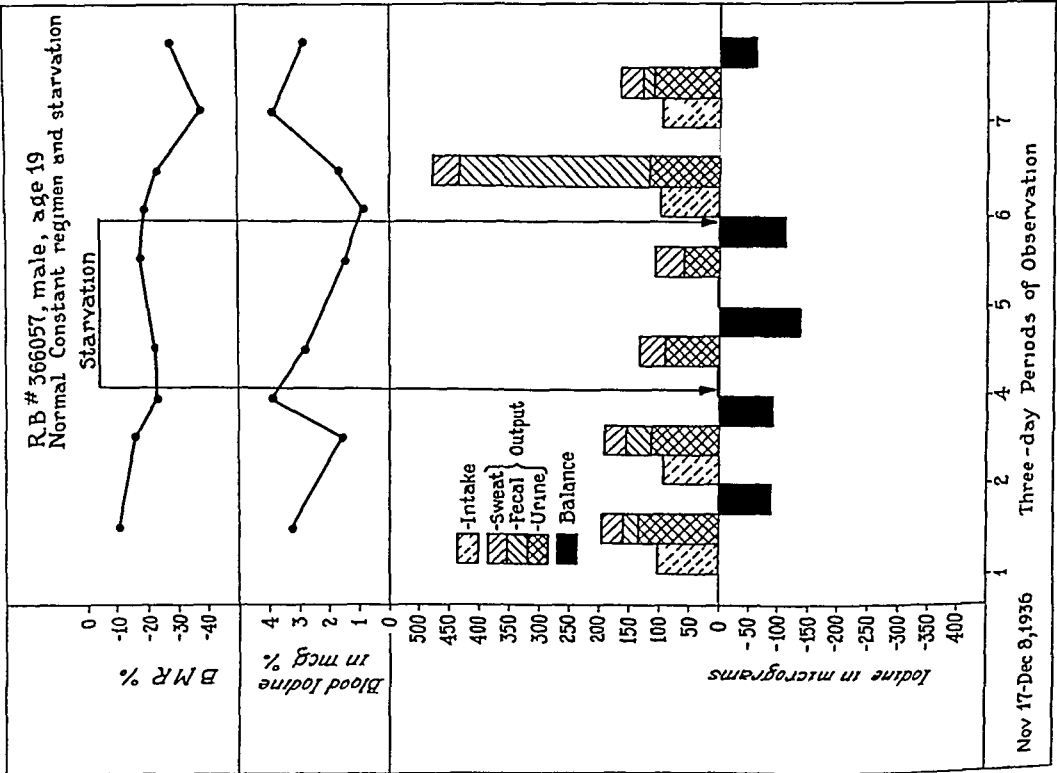


CHART 2—The effect of starvation on the normal iodine balance. Note the continued negative balance.

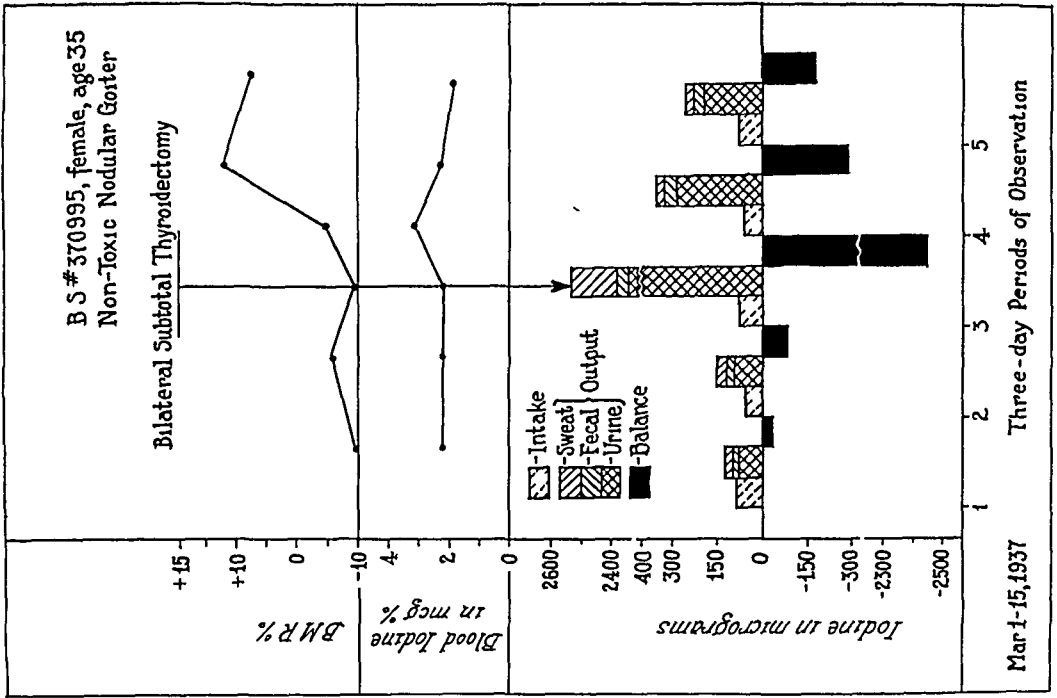


CHART 3—Nontoxic nodular goiter presents a normal negative iodine balance on a low iodine intake. Note the effect of thyroidectomy.

in the decrease in the thyroid gland iodine and in the greatly increased negative iodine balance

Patients with exophthalmic goiter, maintained on a low iodine intake, lose from two to three times the amount of iodine lost by normal persons or by patients with nontoxic nodular goiter similarly controlled (Table II) Thus, the intake of three exophthalmic goiter patients averaged also 29 micrograms

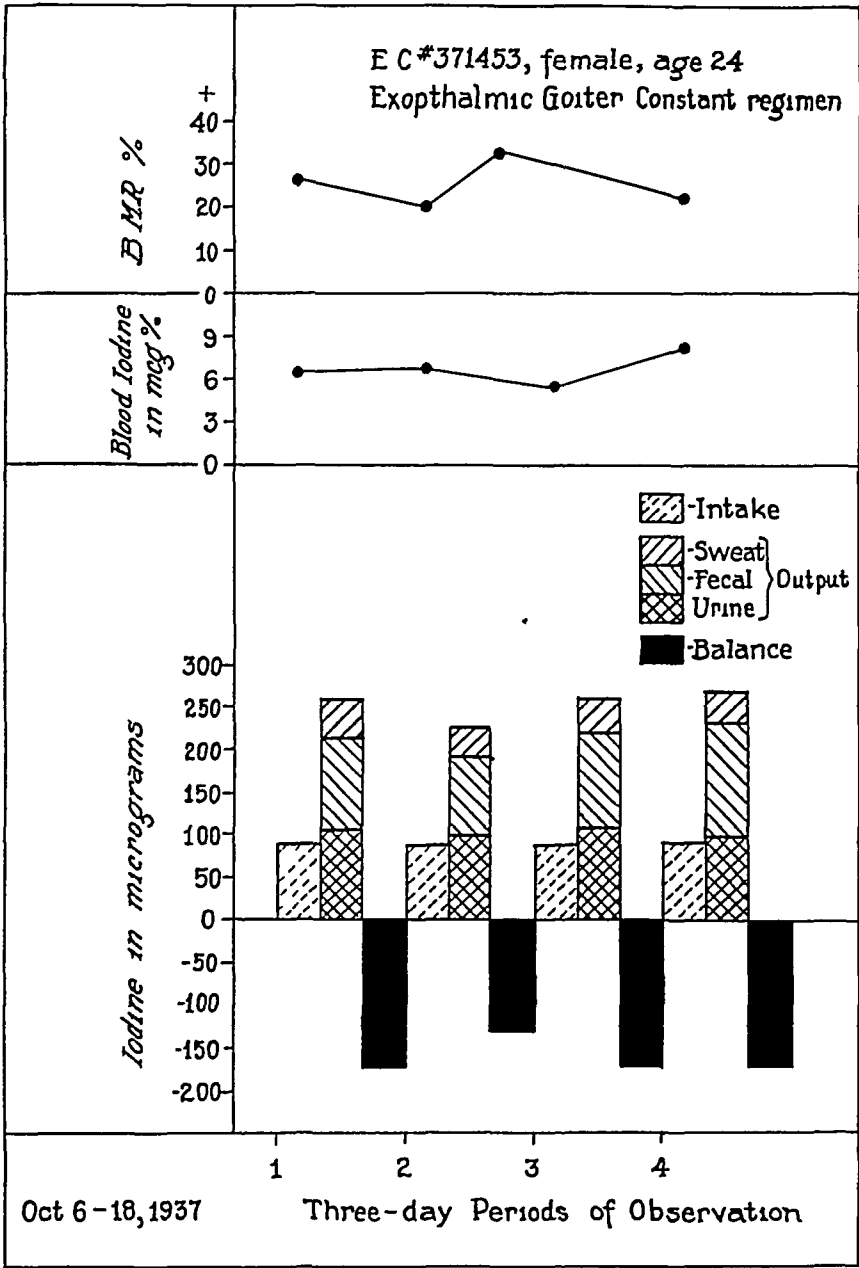


CHART 4—The increased negative iodine balance of exophthalmic goiter
Note the increased fecal excretion over normal

daily, while the daily loss was 138 micrograms This resulted in a daily increased negative iodine balance of 109 micrograms The greatest excretion of iodine was by way of the urine, averaging 49 per cent Forty per cent was lost in the feces and 11 per cent in the sweat The greatly increased fecal loss over normal is shown in Chart 4

It would consequently appear that untreated exophthalmic goiter is characterized by a tendency to lose iodine. Thus, two patients have been maintained on an iodine intake sufficient to keep a normal individual in positive balance, and to allow for some storage. Both, however, showed a continued negative iodine balance^{6, 12}

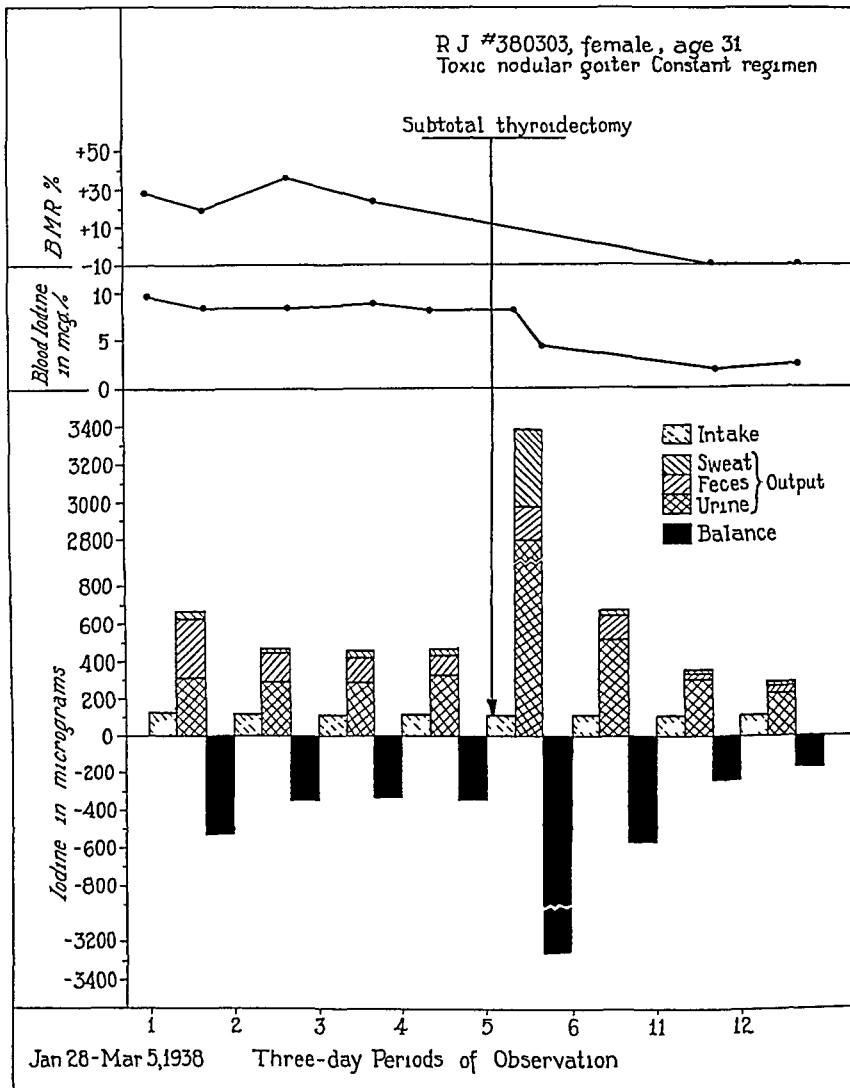


CHART 5—The increased negative iodine balance of toxic nodular goiter. Note the increased urinary excretion over normal. Note the effect of thyroidectomy.

Nevertheless, greatly increasing the intake results in an immediate retention of iodine. Moreover, the resultant positive balance becomes considerably greater than normal (compare Chart 6 of reference 6 with this Chart 1). The diffuse hyperplastic goiter, progressively depleted of iodine during the previous course of the disease, may then rapidly store more than 100 mg. Presumably there is also a lesser repletion of other depleted tissues. This increased storage is maintained for a varying period of time, depending upon the extent to which previous depletion had occurred. However, with the

cessation of the daily administration of 10 mg of iodine, the former negative balance is soon reestablished, while the stored iodine is then progressively lost.⁶ It appears difficult for a patient with untreated exophthalmic goiter to store or to hold iodine.

The true nature of this increased negative iodine balance of exophthalmic goiter needs further investigation. Other tissue-iodine than that of the thyroid gland may play a part. Too, it is possible that iodine has another function in human metabolism besides furnishing two-thirds of the active thyroid hormone, thyroxin. Presumably, however, the increased iodine loss results from an increased secretion and consumption of thyroid hormone with the consequent greater mobilization and excretion of iodine. This problem has been further discussed elsewhere.⁶

Several factors may influence the increased loss of iodine in exophthalmic goiter. On medical management alone, including hospital control with bed rest, a high caloric diet and calcium therapy, one patient showed a remission of the clinical symptoms, and a decrease of the basal metabolic rate to within normal range. There was a corresponding decrease in the excretion of iodine through the various channels, while the iodine balance returned to within normal limits during the sixth three-day period.⁶

Subsequent to adequate thyroidectomy we have found that the disturbed iodine metabolism of exophthalmic goiter returns to normal.⁶ The blood iodine decreases. There ensues a lessened urinary excretion of iodine, while the fecal and sweat loss are also diminished. The increased negative balance decreases, and eventually comes to lie within the normal range. This may ensue as early as the sixth postoperative day.

In conclusion, we wish to compare the disturbed iodine metabolism of toxic nodular goiter with that of exophthalmic goiter. This will be done briefly, since it has been considered *in extenso* elsewhere.⁷ In both, the blood iodine is usually increased, however, in average more so in exophthalmic goiter.⁴ In both, the urinary iodine is usually increased, however, more so in toxic nodular goiter.⁵ Both present an increased fecal and sweat loss, greater in exophthalmic goiter (Table II). In both, the B M R is usually increased, to a higher range in exophthalmic goiter.

Toxic nodular goiter is thus likewise characterized by an increased negative iodine balance,⁷ which is greater than that of exophthalmic goiter. Too, this also returns to a normal range subsequent to an adequate thyroidectomy (Chart 5).⁷

A summary of our balance studies on ten patients^{6, 7} is presented in Table II. This reveals, by comparison, the increased negative iodine balance of exophthalmic goiter.⁶ However, patients with toxic nodular goiter present an even greater negative iodine balance,⁷ due to a greater urinary excretion.⁵ Nevertheless, the excretion of iodine in the feces and sweat is greater in exophthalmic goiter.⁶ These findings have a direct bearing upon the comparative differences between these two forms of hyperthyroidism.

CONCLUSIONS

Exophthalmic goiter is characterized by an *increased mobilization of iodine*. This is revealed in the elevated blood iodine, and by the increased loss of iodine in the urine, feces and sweat. As a consequence of this increased mobilization, *iodine depletion* ensues. This is demonstrated by the decreased thyroid gland iodine and in the negative iodine balance, which is greatly increased over normal. Exophthalmic goiter thus presents a profound disturbance of iodine metabolism.

There is a striking similarity between the disturbed iodine metabolism of hyperthyroidism and the disturbed calcium metabolism of hyperparathyroidism.

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DISCUSSION — DR FRANK H LAHEY (Boston, Mass.) This problem of iodine metabolism is a very interesting one and we have always been interested in Doctor Curtis' investigations. We have carried on some investigations during the past three years in association with Mr Perkin, a biochemist, and have learned some very interesting and valuable things.

When one realizes the variation in tissue iodine content, it becomes evident, at once, what an important part the thyroid plays in this iodine problem. For instance, Mr Perkin has made iodine determinations of 10 Gm of wet tissue and when the 10 Gm of brain or any of the remainder of the tissue is approximately 23 micrograms, not infrequently there will be 3,500 micrograms of

iodine in the thyroid That evidences what a part the thyroid plays in iodine metabolism

We have tried, for a long time, various methods of demonstrating circulating thyroxin, such as the effect of the serum of the patient with hyperthyroidism upon an electrocardiogram of the six, seven, eight or nine day chicken embryo heart, and we have never been able to demonstrate it We have been interested in blood iodine, of course, as a possible indicator of the amount of thyroxin in the blood stream because 65 per cent of thyroxin is iodine The iodine fraction is separable and when separated, thyroxin, of course, no longer elevates metabolism

It has seemed to us, probably in the beginning before we had some of our disappointments, that when a patient had a high blood iodine preoperatively and low postoperatively, which correlates quite accurately with the basal metabolism, that this was probably evidence of the fact that blood iodine is circulating thyroxin, but we have found that 30 per cent of our cases do not have a high preoperative and low postoperative blood iodine They did always, however, have a high preoperative metabolism Thirty per cent of our cases have had a blood iodine preoperatively below normal or normal, which postoperatively went above normal and did not come back to normal for six months Then we found ourselves a little confused

I would like to present on the other hand, certain interpretations which have proven of great value to us I would be very much interested to hear from Doctor Curtis what happens to the urinary iodines in these patients who have low blood iodines in the presence of high metabolism

We have correlated the basal metabolism and blood iodine preoperatively in 110 proven cases of hyperthyroidism, and have charted the course of both of these figures postoperatively at the end of three months and at the end of six months In these cases, the average basal metabolism was plus 45 and the average blood iodine 22.8 micrograms, normal in this region being 10 micrograms At the end of three months the basal metabolism had come to normal, the blood iodine to 10 micrograms, and at the end of six months the basal metabolism was at normal and the blood iodine 7.5 micrograms It is of interest in this group of cases, in which there is the typical preoperative elevation of blood iodine and return to normal correlated with basal metabolism, to note what the percentage of recurrent hyperthyroidism in this group is We are particularly interested in this because by means of blood iodine we can, with quite definite certainty, establish in what cases recurrence is most likely to occur In this typical group with preoperatively elevated blood iodines, there is but one-half of 1 per cent recurrent hyperthyroidism This type of preoperative elevation of blood iodine correlated with basal metabolism both preoperatively and in postoperative drop, represents 70 per cent of all the cases

On the other hand, in 30 per cent of the cases, there is quite a different picture The preoperative metabolism is high but the preoperative blood iodine is not only not elevated, but is below normal At the end of three months the preoperative metabolism has come to normal, but at this time the blood iodine, previously below normal, has now risen to above normal At the end of six months the metabolism remains normal, and at that time the blood iodine has become normal It is in this group of cases that one must look for the recurrent hyperthyroidism because 22 per cent of these cases show a recurrence of hyperthyroidism

When one realizes that our incidence of recurrent hyperthyroidism has been but 3 per cent and that 22 per cent of this group show recurrence, it is

obvious that it is in this group that very radical removals of the thyroid must be performed

There is another interesting clinical observation in connection with the patients who have low blood iodines and high metabolisms, and that is that in the group having high metabolisms and high blood iodines, but 17 per cent required multiple stages, while in the group having high metabolisms but low blood iodines, 45 per cent required multiple stage operations. It is, therefore, as important to realize that not only does this atypical group represent the patients in whom recurrence is most likely to occur, but also the group in which mortality is most likely to occur and in which cautious operative approach must be undertaken.

Another interesting development which has been demonstrated by Mr Perkin in connection with blood iodine is that if one makes a scatter chart of patients' blood iodine in relation to the length of time which they have had the disease, it will be found that in a predominating majority of cases, the blood iodine will be elevated above normal when the disease has been present for a year or less but as soon as the disease has been present for a year or more, a predominating majority of the blood iodine determinations will be found to be below normal. This phenomenon is undoubtedly related to exhaustion of the patient's store of body iodine when the disease has existed a sufficient length of time.

As regards Doctor Smith's paper, we think we will probably always perform thyroidectomy more or less by rule of thumb. It will never be possible, I believe, due to the anatomic variations, the way the lobes go behind the trachea and in the groove between the trachea and the esophagus, to make very accurate decisions about the percentage removed.

There are some very valuable points, however, in this connection, that is, how much thyroid to remove in relation to the patient's reaction to iodine. Doctor Cattell, some years ago, reduced 400 thyroids, surgically removed, to a powder and determined the milligrams of iodine per gram of dried gland, correlating this with the histologic picture, that is, the degree of iodine involution. He found that 90 per cent of the thyroid gland would involute and about 10 per cent would not. He found that the very severe cases were those with small thyroids which were very vascular, very soft and did not involute. You can tell pretty well clinically which patient has involuted and which patient has not, and you can tell very definitely at the operating table which patient has involuted and which patient has not.

The patient whose thyroid gland has involuted under iodine will develop firmness in the thyroid gland, and they will show a drop in metabolism, a gain in weight and a drop in pulse rate. The patients who do not show an involution of their thyroid glands do not show these improvements, and at the operating table when you cut the thyroid gland across, the one that is involuted is pale, firm and nonvascular, the one that has not involuted is red, cellular and vacular. It is in the very small, red, vascular cellular gland that has not involuted that radical removals must be performed if one wishes to prevent recurrence of the hyperthyroidism, and it is in the glands that are pale, firm and nonvascular, and the patients who show marked drops in metabolism, gain in weight, drop in pulse rate after the administration of Lugol's solution, that less radical removals of thyroid tissue need be performed.

DR GEORGE M. CURTIS (closing). We have also observed low blood iodines in patients with exophthalmic goiter, however, our incidence is not so high as that which Doctor Lahey reports. Too, we have noted a low

urinary excretion of iodine in certain patients with exophthalmic goiter. That is also unusual, I should estimate less than 20 per cent.

Doctor Lahey's "scatter chart" has shown a general decrease in the blood iodine as the disease progresses. On the basis of our studies, a part of which have been presented here, this might have been predicted, since the increased mobilization of iodine in exophthalmic goiter eventually leads to iodine depletion. The increased mobilization is shown in the increased blood iodine, and in the greater than normal iodine loss in the urine, feces and sweat. The resultant iodine depletion is demonstrated by the decreased thyroid gland iodine and particularly by the increased negative iodine balance. Patients with exophthalmic goiter thus progressively deplete themselves of iodine in a similar manner as patients with hyperparathyroidism deplete themselves of calcium.

If we could visualize the onset of exophthalmic goiter, it would appear to commence in a normal thyroid gland with a normal iodine content. Precisely what institutes the hyperplasia or what causes the alveoli progressively to lose colloid and consequently iodine, is not clear. Nevertheless, as the disease continues, depletion ensues and increases. Since Baumann's observations, in 1895, it has been known that the iodine store of the diffuse hyperplastic goiter becomes diminished.

By hypothesis, the "scatter chart" appears to present a similar story of progressive iodine depletion as reflected in the blood iodine. We would expect a similar change in the urinary excretion. The severity of the disease and its duration both modify the variable amount of iodine depletion. If this is severe and if resultant damage has followed, it may explain the tendency of patients with low blood iodines to have recurrence.

MEDIASTINITIS FOLLOWING CERVICAL SUPPURATION

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INFECTION of the mediastinum may originate from so many different sources and have such divergent manifestations that the term "mediastinitis" means little unless qualified by a description of its type and kind. The process may range from a simple, nonsuppurative inflammation in association with pericarditis, bronchitis, influenza or pneumonia to a very grave, often lethal, diffuse suppurative phlegmon. A chronic variety is seen in tuberculosis which is sometimes called mediastinopericarditis. Tuberculosis also involves the tracheobronchial lymph nodes with occasional suppuration to form a tuberculous mediastinal abscess. These same nodes are infected in many upper respiratory infections, and should they suppurate, a pyogenic mediastinal abscess results. This phase of the subject has recently been emphasized by Leiche³⁵. Pyogenic abscesses also follow invasion of the mediastinum from contiguous lung abscesses, empyema, cervical infection, spondylitis, perforating wounds or retroperitoneal infection. These abscesses usually develop slowly enough to allow time for diagnosis, localization and drainage. They have been cured by spontaneous rupture into the trachea or esophagus, repeated aspirations by needle puncture, dorsal mediastinotomy, sternal trephine or cervical drainage. In contrast, a mediastinal phlegmon spreading through so vital a spot may be quickly lethal unless strenuous efforts are undertaken for its control. This diffuse suppuration of the mediastinum may come from any of the sources causing localized abscess if the speed and magnitude of the contamination is sufficient, but the visceral perforations of chest and neck are its commonest cause, and of these the cervical lesions are the most frequent. The consideration of diffuse suppurative mediastinitis might well begin with a study of infections in the neck that gravitate into the mediastinum. This demands a knowledge of the fascial spaces connecting the two, for the infection travels along these and it is in them that the surgeon must intercept or drain it. The spaces lie between layers of the cervical fascia, a structure that is so complex that if followed through all of its ramifications is apt to resemble a maze. The subject may be greatly simplified by considering only that part of the cervical fascia and its spaces which significantly relates to the spread of infection. For this purpose it is sufficient to deal with the viscerovascular compartment which contains the visceral space in the center and around it, the prevascular space, the retrovascular space and the vascular sheath on either side.

The first experiments designed to study the compartments of the neck were undertaken by Bichat². But many years elapsed before an intensive

investigation by injection methods was made by Henke,²¹ König and Riedel,²⁷ Soltmann,⁶¹ Poulsen⁵⁴ and Schmitt.⁶⁰ During this period, from 1872 to 1893, most of the essential facts were obtained about the cervical fascia, and the manner of dependent spread of infection along its spaces. For no apparent reason, much of this information has not been referred to in the current literature and references to it are frequently lacking. Some years ago, personal interest in the matter led to anatomic and postmortem dissections in order to study the paths of dependent spread of cervical infection. In doing these the articles of Mosher,⁴⁴ Fuistenberg¹⁰ and Iglauer²³ were helpful. Recently Coller and Yglesias⁷ have reported anatomic studies on this subject.

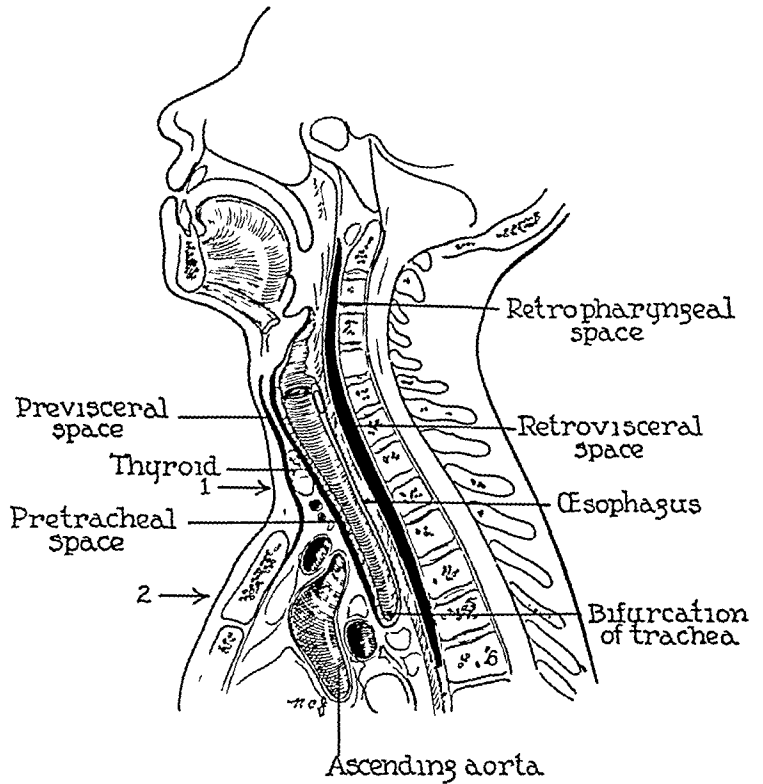


FIG 1—A longitudinal section to show the cervical spaces. In front is the prevertebral space which ends at the sternum and does not enter the mediastinum. Next is the pretracheal space which conveys infection from tracheal and thyroid gland operations. Behind is the retrovisceral space the route traveled by pus in 71 per cent of cases of mediastinitis from cervical suppuration. Note that the retropharyngeal space is not separated from it but is only its upper portion. Numerals indicate the level of cross section for Figures 2 and 3 of the text.

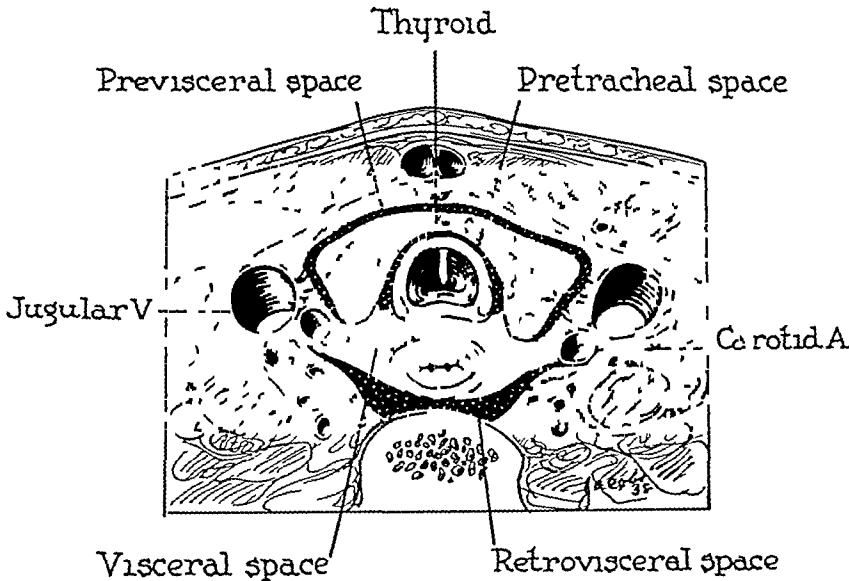


FIG 2—A cross section at the level of the thyroid gland. The visceral space including esophagus, trachea and thyroid gland is a compartment surrounded by the pretracheal fascia in front and the buccopharyngeal fascia behind. In its pretracheal portion is a true space. Behind is the retrovisceral space. Note its relation to the esophagus and cervical spine.

The following summary is an attempt to appraise the facts obtained from the literature in the light of clinical observation and anatomic dissection

THE VISCEROVASCULAR COMPARTMENT—That part of the neck occupied by the pharynx, larynx, trachea, esophagus, thyroid and thymus glands, nerves and great vessels is often termed the viscerovascular compartment. It

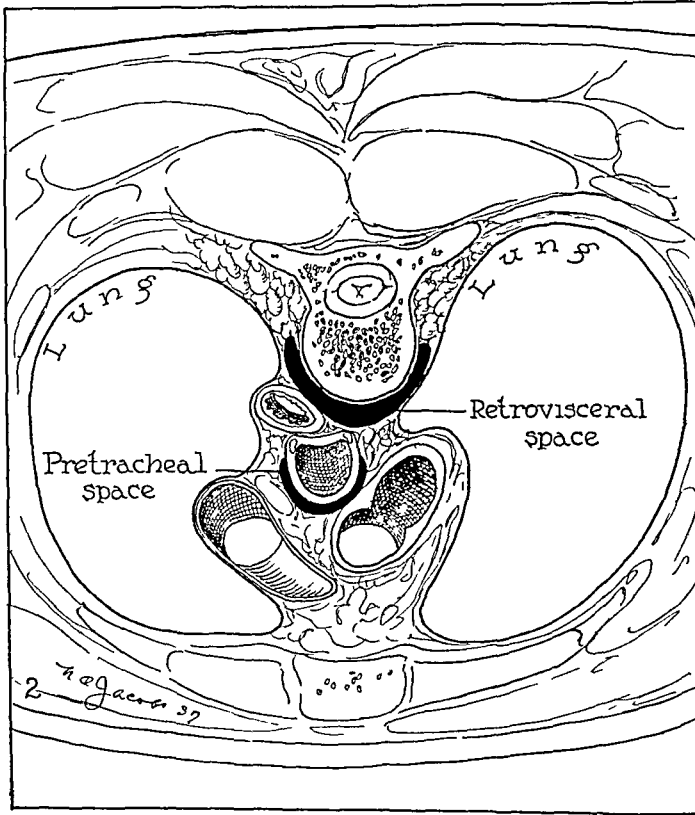


FIG 3—Section in the chest at the level of the fifth dorsal vertebra. The retrovisceral space is in close relation to the pleura.

extends from the base of the skull to the mediastinum where it ends by fusion of its fascial structures about the bifurcation of the trachea, the aorta, innominate vein and pericardium. The consideration of this area as a compartment is for the purpose of orientation, since only in its subdivisions are found actual or potential open spaces. These are shown in longitudinal section in Figure 1, and in cross-section, at two levels, in Figures 2 and 3. Reference to these figures will help to clarify the following description.

Visceral Space—The area bounded by the pre-

tracheal fascia in front, the vascular sheath laterally, and the buccopharyngeal fascia behind, which contains the trachea, esophagus, thyroid gland and nerves, is called the visceral space. It is more potential than real, even though its fascial envelope is one continuous layer. The pretracheal fascia which forms its anterior boundary extends from the hyoid bone to the pericardium, splits to enclose the thyroid gland, then merges laterally with the carotid sheath. The same layer is continued behind the pharynx and esophagus as the buccopharyngeal fascia.

In the anterior portion of this compartment, between the posterior leaf of the pretracheal fascia and the trachea, is a free space, often called the pretracheal space, which extends from the larynx to the bifurcation of the trachea. It has no connection with the spaces in the floor of the mouth or those about the pharynx, so does not convey infection from them. The pretracheal space is usually open during the course of a thyroidectomy, and should infection follow the operation, it may gravitate into the mediastinum through this channel. In performing a tracheotomy the space would seem to be contaminated, yet

mediastinitis from this source rarely occurs. Perforating wounds of the larynx and trachea or operations upon these structures may open and contaminate the pretracheal space, with resultant gravitation of infection into the chest.

In Figures 1 and 3 it is seen that the mediastinal portion of the pretracheal space lies behind the great vessels between the arch of the aorta and the trachea. It is apparent that a surgical approach through the sternum would be difficult because of the interposition of these vessels. The approach through the neck entering the space in the suprasternal notch, below the thyroid isthmus, permits its drainage with the least manipulation. Should the mediastinitis follow thyroidectomy, tracheotomy or other operative procedures in this region, then immediate opening of the wound for drainage should be done.

Infection in the visceral space outside of its pretracheal compartment rarely leads to mediastinitis. The fibrous attachments about the vascular sheath, between trachea and esophagus and between the buccopharyngeal fascia and esophagus impede gravitation of the infection. The usual result is a localized abscess. This is most often seen in perforations of the anterior or lateral walls of the esophagus where, instead of a diffuse spreading infection, one finds a localized suppuration requiring only drainage for cure.

The Previsceral Space—This compartment is familiar to surgeons as the space used in freeing the thyroid gland at operation. It lies beneath the strap muscles and in front of the pretracheal fascia and thyroid gland, extending from the attachment of the sternothyroideus on the thyroid cartilage and trachea down to the manubrium. Furstenberg¹⁰ has emphasized the importance of a process of the pretracheal fascia which attaches to the posterior surface of the sternum and effectively blocks the lower end of the previsceral space. This important attachment prevents infection from reaching the mediastinum.

Carotid Sheath—There is a difference of opinion as to the importance of this structure in conveying infection into the mediastinum, for on the one hand Mosher⁴⁴ says "the carotid sheath is the natural highway for pus and for the surgeon in pursuit of pus", while Parsons⁵¹ does not think the sheath exists until it is "manufactured with the scalpel". It is immaterial whether the pus is considered to run down a closed sheath or to burrow along the loose areolar tissue beside the vessels, for in either event the vessels act as a guide for its descent. The infection may arise from a suppurative adenitis of the deep chain of lymphatics in this region or from a suppurative thrombophlebitis of the internal jugular vein. An equally important source is from inflammation in the parapharyngeal space, a triangular cone-shaped compartment with its base at the skull and its apex ending around the carotid artery (Fig. 4). This space may be contaminated from a needle puncture in performing a tonsillectomy under local anesthesia, or tooth extraction with nerve block, or it may be invaded from a dental abscess in the second or third molar. From Figure 5 it is apparent how a parotid, peritonsillar or retropharyngeal abscess may rupture into it. Any of these causes of parapharyngeal

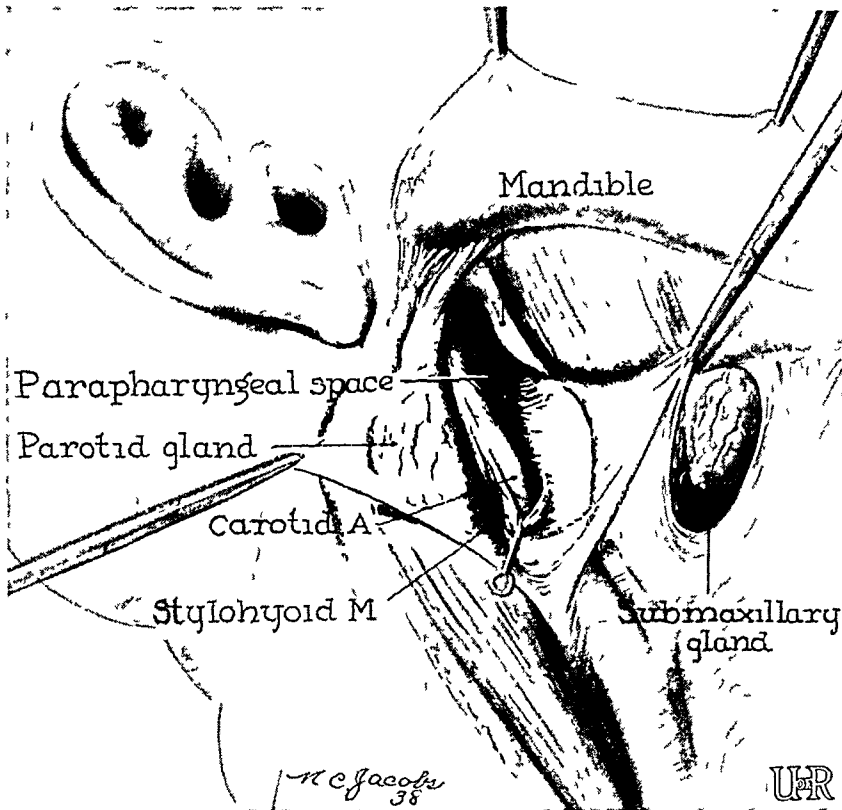


FIG 4.—The parapharyngeal space seen from the outside. The fused fascia is left in front to separate it from the submaxillary space. The parotid gland is turned back in this dissection for exposure. This could not be done so widely at operation without facial nerve injury. The parapharyngeal space extends up behind the angle of the jaw and ends below around the carotid artery.

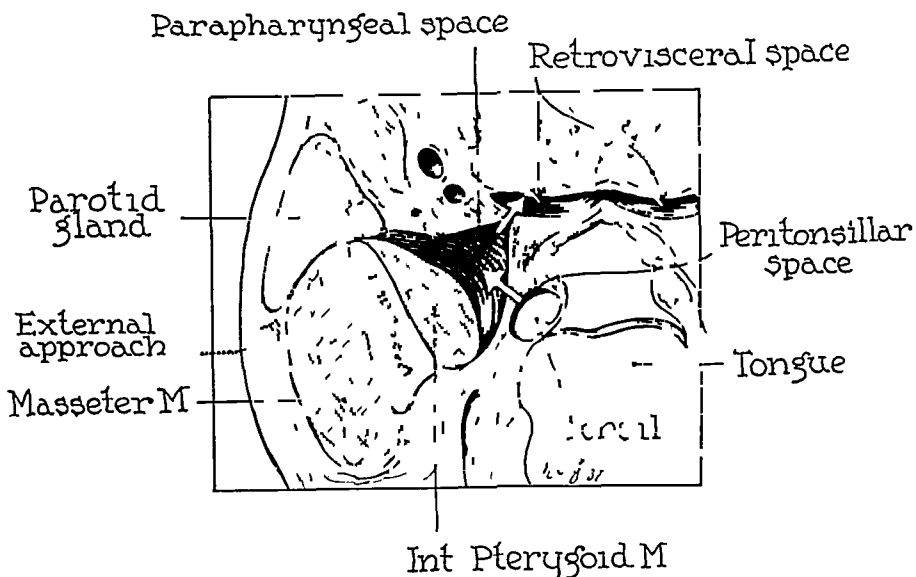


FIG 5.—The parapharyngeal space may be invaded from a tonsillar, parotid or retropharyngeal infection. Pus from this space may track down the carotid sheath or rupture into the retrovisceral space to involve the mediastinum. (This figure is reprinted through the courtesy of the Journal of the Missouri State Medical Association.)

space infection may result in mediastinitis by gravitation of pus down along the great vessels. Should this occur, warning is given by a rise in temperature and pulse and by tenderness in the neck.

Another pathway from the parapharyngeal space to the mediastinum is by rupture into the retrovisceral space. When this occurs it may be difficult to detect, as was learned to our sorrow in one patient with peritonsillar, parapharyngeal infection who developed mediastinitis without showing any signs in the neck.

Gravitation of pus along the carotid sheath to invade the mediastinum may occur very rarely in Ludwig's angina. This infection involves the sublingual-submaxillary space (Fig. 6) which is closed so completely by muscle or fascia

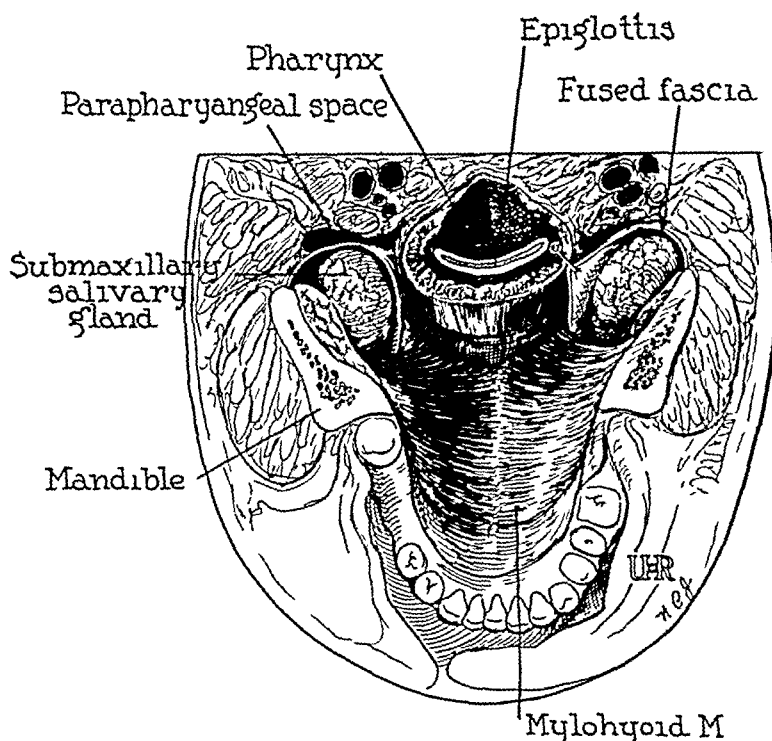


FIG. 6—The sublingual submaxillary space which is involved in Ludwig's angina, is shown by a section through the mouth with the tongue removed. It is separated from the parapharyngeal space behind by the fused fascia which must be eroded through before the infection can gravitate down the neck by this channel.

that no preformed avenue of escape exists. In late, neglected cases the fused fascia may be eroded, allowing drainage of pus into the parapharyngeal space and so down the great vessels or, as was shown by Poulsen,⁷⁴ the infection may rupture out along the facial vessels and follow them to the carotid sheath. Both of these possibilities are remote, and in Ludwig's angina the toxemia from infection or respiratory obstruction is more to be feared than mediastinitis.

Retrovisceral Space—The space behind the pharynx and esophagus is the most important highway of communication between the neck and chest, for it is the route traveled by infection in 70 per cent of the cases. It is bounded by the buccopharyngeal fascia in front, the prevertebral fascia behind, and the carotid sheaths laterally, and extends from the base of the skull to the bifurcation of the trachea. Its lower limit is usually at the level of the sixth dorsal

vertebra, where it is closed by the fibrous tissue about the tracheal bifurcation. Below this obliterated point the space continues to the diaphragm, but this part is not involved in cervical infection. The thin layer of the buccopharyngeal fascia is the only structure separating the pharynx and esophagus from this cavity, therefore, perforation of the posterior wall of these viscera permits direct contamination of the space. This initiates a most rapidly progressive form of mediastinitis, for repeated swallowing forces food, fluid, air and bacteria through the perforation, which mechanically distends the retro-

visceral space from top to bottom. In a matter of hours, it may be filled with infected material. The extravasated air can be demonstrated roentgenologically, as is shown in Figure 7, which is a lateral roentgenogram of the neck in a patient with an esophageal perforation.

The retrovisceral space may also be contaminated by an osteomyelitis or tuberculosis of the cervical vertebrae, in which the infection has eroded through the prevertebral fascia. It has been stated that pus in the parapharyngeal space occasionally ruptures into the retrovisceral space rather than following its usual course down the carotid sheath. Another cause of involvement is from gravitation of a retropharyngeal abscess. The retropharyngeal space is only the upper part of the longer retrovisceral compartment.



FIG 7—The retrovisceral space is defined by air which has escaped into it through a perforation of the esophagus. The upper arrow shows the retropharyngeal part of the cavity while the lower arrow points to a diffuse emphysema in the space.

ment and has no true separation from it. At first glance, one might wonder why retropharyngeal abscesses remain so localized in this free space, but when it is recalled that they begin as a suppurative lymphadenitis, it is apparent that the slow development of the inflammation allows it to seal off from the lower part (Fig 8). Should this obstruction weaken, there is nothing to prevent the infection from sinking into the mediastinum.

INCIDENCE OF SUPPURATIVE MEDIASTINITIS—The foregoing discussion deals with those cervical infections that may cause mediastinitis and the paths they may take to get into the chest. The question arises, how frequently does this happen? Haile¹⁶ states that in 520 cases of mediastinal lesions, consisting of benign or malignant tumors, lymphomata, cysts and infections, there were 78 cases of pyogenic suppuration. The majority were from traumatic wounds penetrating the chest or from intrathoracic suppuration and only 17 came from the descent of cervical infection. Using these statistics

as criteria, we find that pyogenic suppuration causes 15 per cent of mediastinal lesions, and that 22 per cent of these infections gravitated from the neck

The question next arises as to what cervical infections are most apt to produce mediastinitis and what is the relative incidence of each in its causation. In an attempt to answer this, 110 cases of suppurative mediastinitis following infection of the neck have been studied, of these, 99 were obtained from the literature* and 11 from personal experience. They are grouped in order of relative frequency in Table I

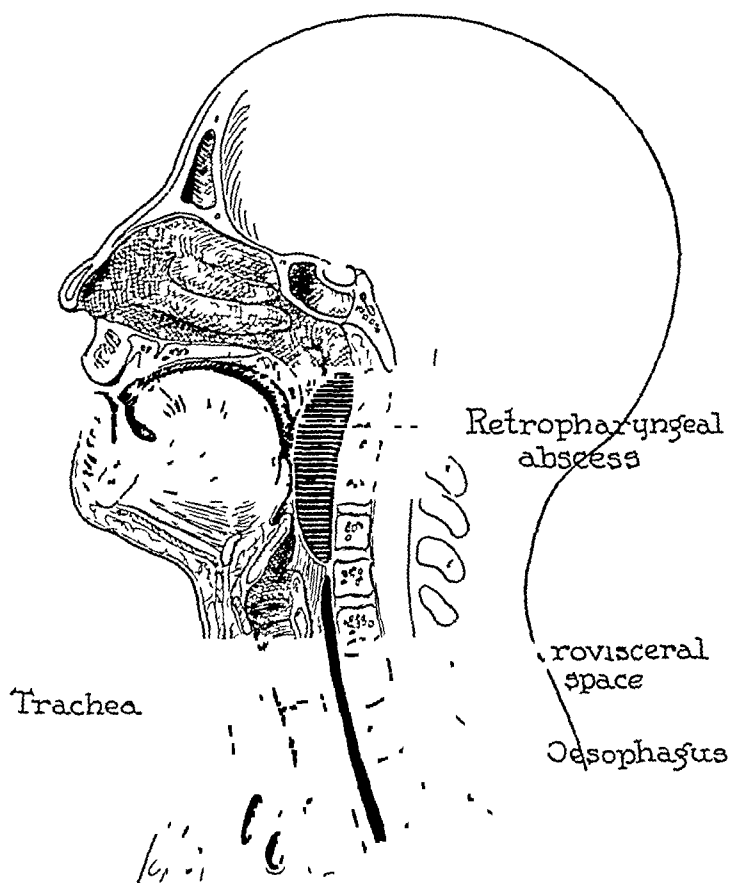


FIG 8—A retropharyngeal abscess occurs in the upper part of the retrovisceral space, but the slow development of the supuration allows walling off of the pus and a separation into two compartments. Should this barrier break, there is nothing to prevent gravitation into the chest

The data in Table I may be regrouped to show the relative importance of the different paths of spread of pus from the neck to the chest. The retrovisceral space conveys infection from perforation of the esophagus, retropharyngeal abscess and spondylitis of the cervical spine. The carotid sheath conducts it in most instances of suppurative lymphadenitis, peritonsillar abscess and Ludwig's angina. The pretracheal space is the course followed in infection after tracheotomy or thyroidectomy. Listed in this way we find them involved as follows: Retrovisceral space 78 cases, or 71 per cent,

*All pertinent articles listed under mediastinum in Quarterly Cumulative Index Medicus were searched for cases. It is probable that this list is incomplete, since some may have been published under titles that would not be filled under this classification. The total number is small but perhaps is sufficient to indicate trends.

carotid sheath 23 cases, or 21 per cent, pretracheal space 9 cases, or 8 per cent

TABLE I
110 CASES OF SUPPURATIVE MEDIASTITIS

Etiologic Factor	No of Cases	Per Cent	Operative Result		Nonoperative Result	
			Recovery	Death	Recovery	Death
Perforation cervical esophagus	64	58 1	24	9	4	27
Suppurative cervical lymphadenitis	13	11 8	7	6		
Retropharyngeal abscess	11	10	6	3	1	1
Peritonsillar abscess	8	7 2	2	2		4
Tracheotomy	6	5 5	1	1	1	3
Spondylitis cervical spine	3	2 8	2			1
Postoperative thyroidec-tomy	3	2 8	1	2		
Ludwig's angina	2	1 8	1	1		
Total	110		44	24	6	36

In a majority of the cases studied the infection came from perforation of the cervical esophagus. Neuhof,⁴⁷ in a report on mediastinal suppuration from both cervical and thoracic sources, found perforation of the esophagus the cause in "almost 50 per cent of the cases." This viscus may be penetrated by external traumatic or surgical wounds, or perforated from within by foreign bodies, bougies, an esophagoscope, or eroded by tumors. The author and Doctor Heatly,¹⁸ in a study on the management of esophageal perforation, decided that immediate external operation is the treatment of choice in order to prevent the occurrence of mediastinal infection and the consequent necessity for its drainage. This view is strengthened by the results of treatment of suppurative mediastinitis shown in Table I. In the 64 cases of perforation of the cervical esophagus, 33 received early operation with nine deaths, a mortality of 27 per cent, while in the 31 cases not operated upon, 27 died, a mortality of 87 per cent.

THE PREVENTION OF MEDIASTITIS—The mediastinitis which follows cervical suppuration results from a dependent spread of infection along the fascial planes. If this gravitation of pus could be blocked, the chest infection would be prevented. Reasoning along these lines, von Hacker¹⁵ proposed a prophylactic operation for packing the spaces in the neck. This procedure was popularized by Marschik,³⁹ and has been described by Palmer⁵⁰ and Glogau¹³ in this country. Recognition of the importance of the retrovisceral space as a path for the descent of pus led to the development of an operation to block it.⁵² These procedures seek to erect a transverse barrier of adhesions across the fascial spaces that connect the neck with the chest. They are indicated in the traumatic visceral perforations, especially of the esophagus.

where the progress of the infection is very rapid. Here, even if the surgeon is too late to interrupt the gravitation, he can drain the space and, by releasing tension, prevent extension to the chest.

There is much less indication for prophylactic block of the fascial spaces in the absence of rapidly spreading infection from a visceral perforation. Most suppurations in the submaxillary-submental, parapharyngeal and retropharyngeal spaces or in the carotid sheath are best attacked directly and drained. If the pus has descended in the neck, it will have done so slowly and should be released without destroying the inflammatory adhesions below it. Dissemination of infection might well follow an attempt to do more than this.

MANAGEMENT OF MEDIASTINITIS—There is every reason to believe that suppuration in the mediastinum should be attacked surgically and drained just as infection in a more accessible location would be. This principle is applicable irrespective of the source of the pus. In the 110 infections which came from the neck, 68 were operated upon with 24 deaths, a mortality of 35 per cent, in contrast to an 85 per cent mortality when operation was not performed. The drainage was accomplished through the esophagoscope in 13, the chest wall in 14 and the neck in 41. There is some controversy among endoscopists as to whether infection should be drained through the endoscope or by external incision. It is probable that the endoscopic approach should be limited to the evacuation of a localized abscess that impinges on the esophagus or presents behind the pharynx.

Incision through the chest wall may be by the anterior or posterior approach. The former is rarely necessary for drainage of infection but the posterior route is useful. The technic of dorsal mediastinotomy is described by Lihenthal,¹⁶ while its historical background is given by Gaudiani.¹² It is the operation of choice in draining suppuration below the level of the sixth dorsal vertebra, and is often advisable in evacuating chronic abscesses of the posterior mediastinum at any level in order to collapse their walls. It is a more formidable procedure than the operation through the neck, which should be used whenever possible.

Cervical mediastinotomy was described by von Hacker,¹⁵ though Lurman¹⁷ reported, in 1876, drainage of a mediastinal abscess that presented in the neck. This operation is the logical approach for drainage of mediastinitis above the level of the sixth dorsal vertebra. That which originates from cervical infection falls in this category and should be so treated, for as Furstenberg¹⁰ states: "To drain an infection through the tissues which it has invaded, is, I believe, a surgical axiom." It has the advantage of allowing direct inspection of the extent and location of the suppuration.

The incision in the neck is usually made parallel to the lower, medial border of the sternocleidomastoid muscle, though it may be placed transversely to follow the skin folds. The sternocleidomastoid is retracted and the fascia lateral to the sternothyroid muscle is divided to expose the carotid sheath and

thyroid gland The lateral, and perhaps the inferior thyroid, veins are ligated and divided This allows lateral retraction of the vessels and medial displacement of the thyroid gland, in order to expose the trachea and esophagus If a short inferior thyroid artery prevents this, it is ligated and divided At this stage the carotid sheath and pretracheal space may be inspected, but if uninvolved, they are not opened and the dissection is carried behind the esophagus This opens the retrovisceral space as is shown in Figure 9 If pus is encoun-

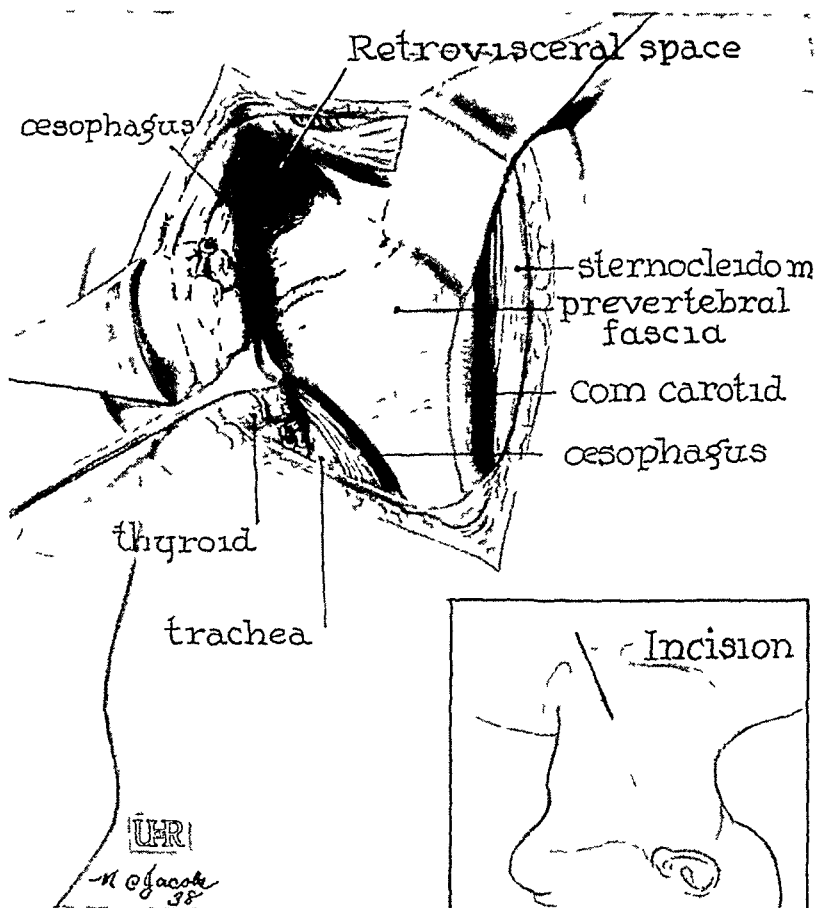


FIG 9—Looking down into the posterior mediastinum through the retrovisceral space, as it is seen at operation. Orientation is easier if the drawing is turned so the head is up. The thyroid gland, trachea and esophagus have been retracted mesially, while the carotid artery, jugular vein and sternocleidomastoid muscle are displaced laterally. This exposure permits visual inspection of the space.

tered, it is aspirated and drains are placed to the bottom of the cavity. Some surgeons prefer the approach behind the sternocleidomastoid muscle, but danger of nerve injury is greater in this location. The important factor is to obtain direct drainage, for failure to do this may allow pocketing and residual abscess formation. If the infection has dependent pockets on either side of the midline, they should be drained through separate incisions on the corresponding sides of the neck. A drain crossing the midline is pinched between the spine and the esophagus and causes obstruction to the drainage and abscess formation as is illustrated in Case 1.

Case 1—Hosp No 85308 A female, age 45, was seen 30 hours after an instrumental perforation of the esophagus. The pain, swelling and emphysema were most marked on the left side of the neck, so the incision was made there. But it was found that dependent pockets were present in the mediastinum on both sides, that on the right being the deeper of the two. The patient's condition was very poor, so drains were inserted into both of these cavities and brought out through the incision on the left side. The plan was to perform a second operation on the right side but the patient was too ill to warrant this procedure. She was comatose and aroused only in delirium. The tempera-

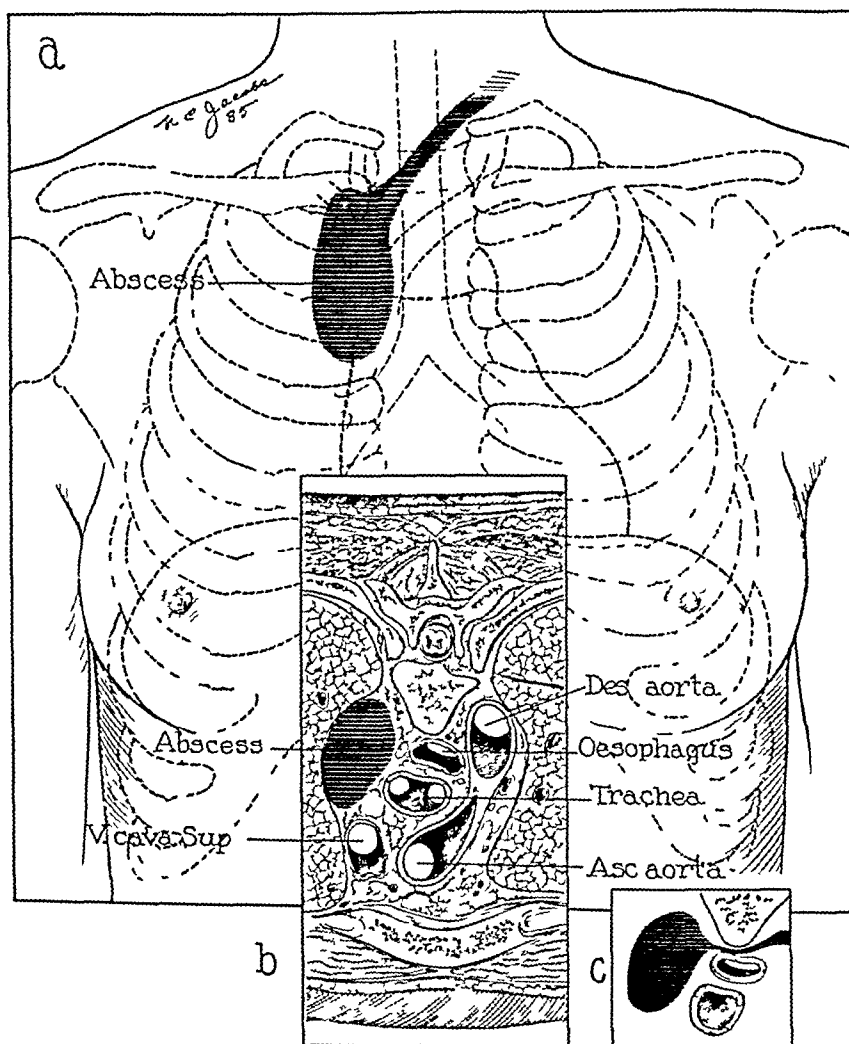


FIG 10—Case 1. Residual mediastinal abscess three months after an acute mediastinitis from esophageal perforation. The location in the vertical plane is shown in (a), and in horizontal section in (b). The pinching of the tract between the spine and esophagus is shown in (c). This caused in complete drainage of the suppuration and allowed the abscess to persist.

ture, pulse and respiration were sustained at a high level. Cyanosis was so marked that an oxygen tent was required constantly. Subcutaneous saline, intravenous glucose, and transfusions were administered, to maintain the fluid balance, while a gastrostomy was performed for feeding. For nine days she held on to life by a narrow margin and then improved rapidly. The fever subsided, mental clarity and physical strength returned and she appeared to be on the road to recovery. Whereas, before she was too sick to drain through the right side, it was now thought that she was too well to need it. This was wrong, for drainage persisted. Injection of the tract showed a residual abscess in the mediastinum. Prolonged attempts were made to drain this by suction through a catheter, but the abscess persisted. Finally three months after the operation for the mediastinitis the abscess was drained through the right side of the neck. The patient died six days

after operation of bronchopneumonia, having survived the acute phase of her illness but succumbing to one of its sequelae

Autopsy revealed a thick-walled abscess cavity, free of pus, situated in the right posterior mediastinum at the level of the aortic arch (Fig 10) The old drainage tract was compressed between the vertebra and esophagus The left side of the mediastinum which had received direct drainage was completely healed

It may be, that it is always more advisable to drain through an incision on the right side, but now after the experience in Case 1, if bilateral pockets are found to exist, both sides of the neck are opened The exploratory incision should be made on the right side, as anatomic relations make this preferable

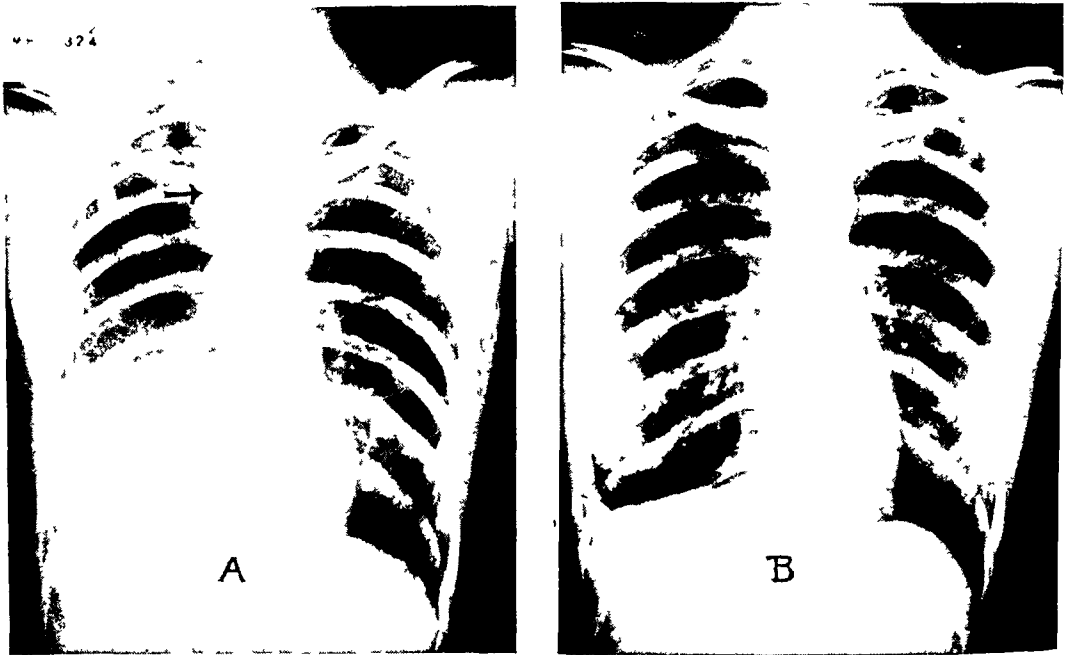


FIG 11—Case 2 (A) The arrows point to a residual abscess which has formed during recovery from acute mediastinitis The pleural edema at the right base is still present (B) The abscess has been drained and the chest is clear

The postoperative care of patients with mediastinitis is important, for they are sick and need much supportive treatment Immediately after operation they should be placed in the Trendelenburg position and kept there until the drainage diminishes or ceases, as otherwise the pus will not run out of the dependent pocket This position becomes tiresome, but if not maintained may lead to a residual abscess, as happened in Case 2

Case 2—Hosp No 56324 A female, age 20, lacerated the cervical esophagus with a clam shell She was operated upon 48 hours after the perforation Pus was found in the posterior mediastinum Drainage was established through the incision on the right side of the neck A gastrostomy was performed the following day for feeding Fluids were forced by subcutaneous and intravenous infusions She ran a septic type of temperature, pulse and respiration for one week and then, as these were subsiding, the head of the bed was elevated slightly Following this the drainage diminished, and the septic phenomena returned A residual mediastinal abscess (Fig 11) was demonstrated on the 13th postoperative day, which was drained by inserting a catheter into it

through the wound in the neck. She was returned to the Trendelenburg position which, combined with aspiration and irrigation through the catheter, resulted in the evacuation of much pus. Her septic course promptly subsided. Drainage ceased at the end of two weeks, and the catheter and gastrostomy tube were removed, feeding by mouth was resumed, and the wound in the neck was allowed to heal. Recovery was uneventful.

This case illustrates the necessity of keeping the patient's head down, in order to provide dependent drainage until the discharge diminishes or ceases.

The mediastinitis which comes from perforation of the pharynx or esophagus may be complicated by the feeding problem. The swallowing of fluids or food, in the presence of an opening in the tract, allows additional extravasation and contamination and should be eliminated. Absolute rest of the esophagus is impossible, for patients will always swallow some saliva. Relative inactivity, however, may be accomplished by employing an indwelling stomach catheter or establishing a gastrostomy. The tube feeding would appear to be the simpler, but it has been tried repeatedly and found to be less satisfactory than a gastrostomy. Artificial feeding is continued until drainage from the mediastinum stops, then liquids and soft solids are tried by mouth before removing the gastrostomy tube. Should an esophageal fistula be suspected, a drink of dilute methylene blue solution will confirm its presence by its appearance on the dressings of the wound in the neck. No difficulty has been experienced with persistent fistula or stricture formation in these traumatic perforations of the esophagus.

The maintenance of an adequate fluid balance is accomplished by the administration of Ringer's solution or glucose given subcutaneously, intravenously or by rectum. Blood transfusion is administered when indicated by the presence of anemia or depletion of serum protein, for either of these may occur in patients who are receiving a low protein intake in the presence of a suppurative infection. Another measure of value is the liberal use of oxygen in the immediate postoperative period, as cyanosis is often present in suppuration of the mediastinum. Some patients show clouding of the lung fields on roentgenologic examination of the chest. This is not ordinarily accompanied by signs of pneumonia and has been attributed to pleural edema. The intimate relation of the pleura and fascial spaces, especially the retrovisceral space, is shown in Figure 3. The pleural reaction with edema varies from a minor degree of thickening to a frank pleurisy and the production of sterile, straw-colored fluid. Repeated examinations have never revealed infection of this exudate and it clears up rapidly with subsidence of the mediastinitis.

The use of the procedures described may be followed by prompt healing if all the factors are favorable. However, in spite of diligent care, some unfavorable circumstances may delay recovery and lead to a protracted convalescence. This is well illustrated in Cases 3 and 4, which are presented for contrast.

Case 3—Hosp. No. 83591. A married woman, age 21, in normal good health, swallowed a fragment of a toothpick which lodged in the cervical esophagus. The foreign body was removed without difficulty through the esophagoscope by Doctor Heath. The

sharp point, however, was so firmly embedded in the posterior wall that perforation was feared. This was confirmed by the onset of progressive dysphagia, pain, tenderness and emphysema of the neck, fever and leukocytosis of 29,000, during the following 24 hours. Cervical mediastinotomy was performed through an approach in the right side of the neck, and a fulminating *Streptococcus mediastinitis* was drained.

Postoperative treatment was given as described except that oxygen was not needed and the establishment of a gastrostomy was delayed, since it was thought to be unnecessary with such a minute perforation. However, on the fifth postoperative day, the presence of material on the dressing, resembling orange juice, led to a methylene blue test which revealed a fistula. Fluids by mouth were stopped and a gastrostomy was performed. The temperature and pulse reached normal on the ninth day, the drainage diminished and finally ceased on the seventeenth day, and feeding by mouth was resumed. Uninterrupted convalescence followed (Fig 12B).



FIG 12—(A) Showing the condition, two days after onset, of a suppurative mediastinal infection from esophageal perforation. (B) The appearance of the chest, ten days later after it had subsided.

This rapid recovery from a virulent infection was no doubt greatly helped by the robust health of this young woman. That the debilitating effect of age and the complication of other disease processes may mitigate against recovery or delay convalescence is well illustrated in Case 4.

Case 4—Hosp No 114,220. A frail woman, age 67, with generalized arteriosclerosis, arteriosclerotic heart disease and cholelithiasis, was admitted for digestive complaints arising from an esophageal diverticulum. Diagnostic esophagoscopy was carried to the opening of the sac but no further. After eating her lunch that day, she developed a chill, fever, leukocytosis, dysphagia, pain, and tenderness, emphysema in the neck soon appeared. A perforation of the esophagus was evident. Operation was performed eight hours after the onset of her first symptom, yet it was found that the retrovisceral space was distended throughout its length with a foul, bloody, purulent fluid containing food particles. This was aspirated out and drains placed to the bottom of the mediastinal cavity. She was placed in an oxygen tent in Trendelenburg position, fluids and blood were given and a gastrostomy established. The temperature, pulse and respiration remained elevated for

25 days, with persistence of drainage from the wound and fistula in the esophagus. The latter was probably continued by the partial obstruction from the diverticulum. Just after her septic phenomena had returned to normal, they rose again in association with right upper quadrant abdominal pain and jaundice (icteric index 50). A diagnosis of common duct stone was made. Fortunately the stone was passed, and the jaundice gradually cleared up during the following nine days. After draining profusely for 40 days, the mediastinal infection began to subside and cleared completely during the next two weeks (Fig 13B).

In this patient, the debilitating effect of age with its degenerative disorders and the complications of the cholelithiasis and esophageal diverticulum materially retarded recovery.

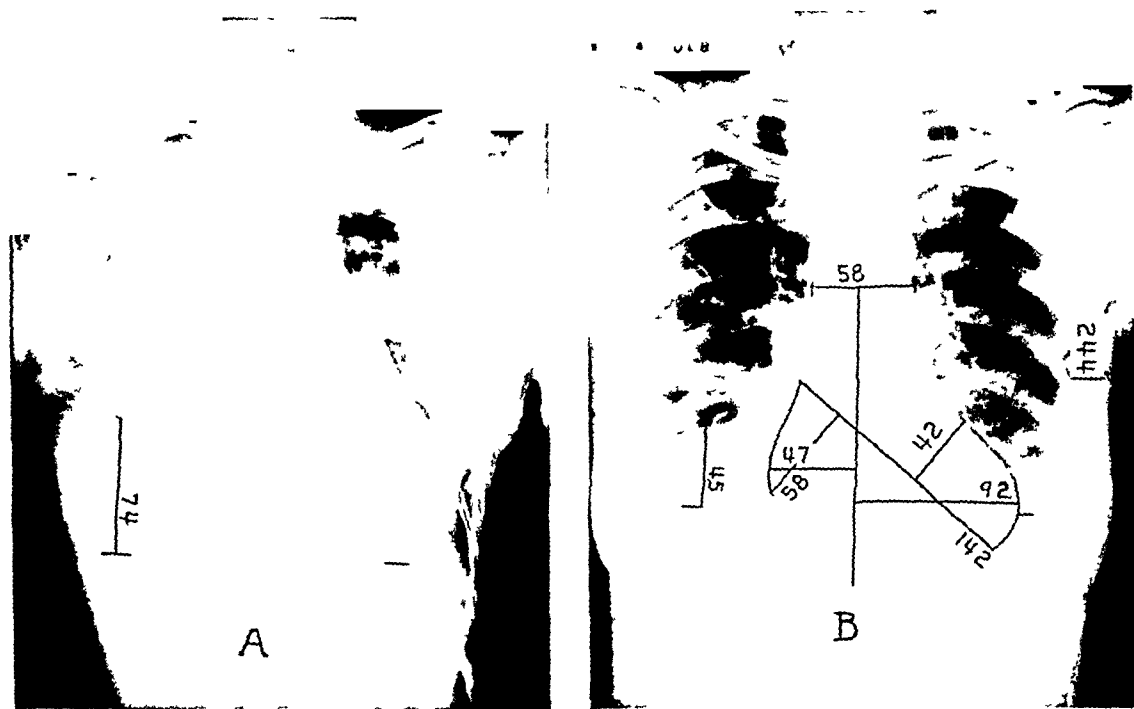


FIG 13—Case 4. In (A) an extensive mediastinitis is shown at its worst while in (B) the process has cleared.

Mediastinitis from cervical sources other than visceral perforation is apt to be slower in its progress and less lethal in its effect. Pus which originates about the mouth or high in the neck, secondary to infection in these regions, tracks down along the fascial spaces slowly enough to give warning. It is often accompanied by an inflammatory reaction in the fascial spaces which produces a barrier to the gravitation of the pus. Care should be used not to break down this barrier at operation, for if it is preserved recovery will be prompt, as is well illustrated in Case 5.

Case 5—Hosp No 105,448. A robust male, age 17, was admitted with an infection behind the angle of the right mandible, which followed a cold and sore throat two weeks previously. The swelling in the neck was associated with temperature of 40° C, chills, dyspnea, dysphagia and inability to open the mouth. It was drained by the resident surgeon, under the impression that it was a submaxillary space abscess, but in retrospect a parapharyngeal space involvement may have been present. Four days after this operation he had a rise in TPR and complained of tenderness low in the right side of the neck. Operation was advised for descending cervical infection. Thick, yellow pus was

found tracking down mesially to the carotid artery. This showed *Streptococcus hemolyticus* on culture. The cavity extended to the upper part of the mediastinum which was sealed off by inflammatory adhesions. Care was used not to break these down in establishing drainage, and he recovered without further difficulty.

DISCUSSION—It would appear that suppurative mediastinitis from descending cervical infection is not always a hopeless condition but is amenable to cure if energetic measures are taken to treat it. This requires familiarity with the anatomic arrangement of the cervical fascia, and its spaces, that connect the neck and chest, in order to execute the surgical procedures that are necessary. Persistence in postoperative treatment is most essential.

Anatomic division of the mediastinum by theoretic planes for descriptive purposes is not of much clinical value. Assistance in the solution of practical problems might be gained from dividing the region into four compartments by two planes: the first, a vertical line, would follow the trachea to create the anterior and posterior portions; the second, or horizontal plane, would be at the tracheal bifurcation or about at the level of the sixth dorsal vertebra. This would place the heart and pericardium in the lower anterior quadrant, while the thymus, pretracheal space, substernal thyroid gland, and aberrant parathyroid tumors would be in the upper anterior quadrant. The posterior portion would contain the esophagus and retrovisceral space, the latter divided into its upper and lower portions. From the standpoint of treating suppurative mediastinitis, this concept is useful, for anatomic barriers limit the infection to these four segments.

SUMMARY

(1) Gravitation of pus from the neck causes only one-fifth of the cases of suppurative mediastinitis; in this group, however, are found many of the more dangerous infections from visceral perforation.

(2) The paths of dependent spread along the cervical fascial spaces are described. It is found that the suppuration followed the retrovisceral space in 71 per cent, the carotid sheath in 21 per cent, and the pretracheal space in 8 per cent of the cases.

(3) The operative procedures for the prevention and treatment of this type of mediastinitis are discussed. Operation is indicated, as with surgical intervention the mortality is 35 per cent as contrasted with 85 per cent when it is not performed.

(4) Cases of suppurative mediastinitis are presented to illustrate the methods of management of this disorder.

The author's appreciation is expressed to Dr Clyde A. Heatly, for having made the esophagosopic examinations, and to Dr Joseph H. Green, for his roentgenologic work, in the cases reported in this series.

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DISCUSSION—DR EDWARD D CHURCHILL (Boston, Mass) Perforation of the esophagus by foreign body, or as a result of instrumentation, is as urgent a surgical emergency as a perforated abdominal viscus. The flora of the lumen of the esophagus is as virulent as that of the large bowel. The proper treatment of perforation of the cervical and upper thoracic esophagus is immediate operation by the cervical approach. Operation should not be delayed for the development of signs of local inflammation or roentgenologic evidence of air in the tissues.

Unfortunately, perforation of the esophagus frequently occurs as one of the tragedies of modern medicine—a dangerous and possibly fatal complication of a diagnostic procedure. A perforation of the esophagus by instrumentation must be handled like a perforation of any other viscus. If a surgeon is so unfortunate as to perforate the sigmoid with the endoscope, he knows what he must face and what he must do. Endoscopists must realize that if they find a perforation from a foreign body or if they are unfortunate enough actually to perforate the esophagus with their instrument, proper treatment must be carried out immediately.

I have used the method employed by Doctor Pearse, in an elderly patient with a chicken bone perforation, demonstrated by esophagoscopy. She was diabetic, and operation was performed within 15 hours of the perforation. There was already foul-smelling, thin pus in the retrovisceral space. Recovery followed.

The virtues of posterior mediastinotomy in approaching abscesses of the retrovisceral space must not be overlooked, and while the cervical approach, as Doctor Pearse has shown, is the method of election in perforations of the cervical esophagus and perhaps the upper mediastinal portion of the esophagus, there will be an occasional case where posterior mediastinotomy should be employed. I have performed this twice, and one of the two patients recovered.

A problem that Doctor Pearse did not touch upon, but concerning which we would like information, is the handling of perforations of the esophagus that occur below the level of the bifurcation of the trachea. After infection occurs, the treatment is obvious, but should immediate mediastinotomy be advised if the case is seen early? Usually such a case is seen only after an empyema has developed secondary to a mediastinitis.

Doctor Pearse brings out the problem of feeding, and states that he per-

forms a gastrostomy in many instances. Personally, I have employed a gastric tube which is inserted on the operating table, while a finger can be kept in the incision, and the tube guided past the point of perforation.

There is one other quite rare route for extension of cervical infection into the thorax. Suppuration arising from cervical lymphangitis in the region of the juncture of the great veins just at the thoracic inlet may, instead of descending medially into the mediastinum, descend laterally, dissecting the parietal pleura from the endothoracic fascia and present in the axilla, simulating an empyema.

DR MARTIN B TINKER (Ithaca, N Y) I would like to compliment Doctor Pearse on bringing before this Association this very dangerous and rather difficult complication which is likely to occur to any of us, particularly those who do much surgery in the neck.

A condition which has come to my notice was not mentioned. Extension down the jugular vein of infection in thrombosis of the lateral sinus. Another case had a perforation of the esophagus by an oyster shell, which caused extensive infection, and two cases of neglected suppurative thyroiditis resulted in a serious descending infection. It is unbelievable how rapidly these infections develop in some instances.

DR HOWARD LILIENTHAL (New York, N Y) This is a matter which, as a thoracic surgeon, has interested me tremendously. I have written a little about it and you will find some points which have been brought out by this excellent paper of Doctor Pearse's in a book that I¹ wrote, which appeared 13 years ago.

Although I have discussed this repeatedly since that time, it appears to me that surgeons in general are afraid of the mediastinum. I believe that if there is a history which points to the possibility of this complication, it is better not to wait, particularly when the patient is very ill. Posterior mediastinotomy is not nearly as dangerous as many seem to believe. If no infection happens to be encountered, there is, with proper precautions, almost no likelihood that it will become infected from the exploration. Posterior mediastinotomy affords an excellent exposure.

I would emphasize one or two points in regard to this form of exploration. (1) If there is a history of endoscopy, especially of the esophagus, one should early suspect involvement of the mediastinum, and one should not fear mediastinotomy by the posterior approach. If the suspected lesion is in the lower part of the esophagus, exploration is just as necessary as when it is in the part with which Doctor Pearse's paper especially deals.

Gunshot wounds may also infect the mediastinum, posterior or anterior, and even operations for goiter have been known to be followed by this complication, although I myself have seen only one. I agree with the speaker about the importance of inverting the patient, but in some instances where this is difficult, a multifenestrated tube placed through the upper wound into the space and equipped with a suction apparatus will be effective. This will often make a secondary procedure unnecessary. It should also be borne in mind that in the lower third of the chest the right pleura often, in fact usually, extends over the midline into the left. Therefore, in opening the lower part of the mediastinum, especially on the left side, beware of the overlapping right pleura, or there may be a fatal infection of both cavities.

Another useful function, if one may so denominate it, of posterior mediastinotomy is the opening of certain lung abscesses which point here. I have done this several times.

Finally, I would urge that the possibility of suppurative mediastinitis should be borne in mind, even though roentgenologic examination does not reveal it

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DR JOHN ALEXANDER (Ann Arbor, Mich) May I offer, as a corollary to Doctor Pearse's presentation, a suggestion as to the choice between cervical drainage and thoracic drainage of these abscesses? I have used both approaches and have been satisfied with both, but I feel one should choose the approach according to the case May I suggest that in those which are operated upon quite early after the beginning of the infection, and are located high in the mediastinum or low in the neck, the cervical approach is obviously the better, but those that have localized as far down as the fifth or sixth thoracic spine, particularly when the case is a relatively old one, let us say more than two or three weeks old, and particularly when there is evidence that some foreign body has lodged in the abscess, a posterior mediastinotomy is the better approach

I feel that in a case that has become subacute or chronic, prolonged cervical drainage through a tube which lies close to the carotid sheath may possibly cause an erosion of the carotid artery and fatal hemorrhage, whereas, prolonged drainage through a wide posterior mediastinal incision, with packing of that incision, presents almost no danger of pressure necrosis of a large vessel

As Doctor Lihenthal has said, the opening of the mediastinum is simple in cases in which there is a large abscess that projects on either side of the spine, or bilaterally The parietal pleura will have been dissected away from the mediastinum by the abscess, so that a resection of two or three inches of two posterior ribs together with the transverse vertebral processes, and a division of the intervening intercostal bundle, permit one to enter the abscess directly If a foreign body has dropped into the bottom of such an abscess, or is imbedded in the soft tissues, it would be difficult to safely remove it if one attempted to do so through the more or less long track which would have been produced through a cervical incision

In summarizing, I suggest the use of a cervical incision in acute cases and in those in which the infection, particularly free pus, has not extended as far as the fifth or sixth thoracic spine, but a posterior thoracic incision for older cases which will probably require prolonged drainage and those in which a foreign body may have become lodged in the abscess in a position that is relatively inaccessible through a cervical incision

DR OWEN H WANGENSTEEN (Minneapolis, Minn) This presentation by Doctor Pearse is an important one There is one point which I should like to make concerning early recognition of perforation of the esophagus Doctors Pearse and Churchill both indicated that there was often much delay between the occurrence of this tragedy and its identification Whereas, considerable time may elapse before subcutaneous emphysema becomes appreciable by palpation, yet, the presence of air in the interstitial tissues about the esophagus can usually be detected in a roentgenogram a few minutes after its escape from the esophagus I would, therefore, strongly urge that all cases in which perforation of the esophagus is suspected have a roentgenogram made immediately of the neck and thorax in order to identify the possible presence of air Such a film can be repeated if necessary after a short elapse of time

A hospital visitor with a self-inflicted bullet wound through the neck, who had shot a hospital patient through the chest, was seen by me several years ago, a short time after the shooting. The offender presented no evidence of hemorrhage or nerve injury and there was no subcutaneous emphysema. He was hustled off to jail and died a few days later, I learned subsequently, from mediastinitis resulting from perforation of the esophagus. Since then, I have looked for evidence of escaped air from the esophagus in a roentgenogram rather than with the palpating hand. In the drowsy small hours of the night, I have once made the diagnosis of spontaneous perforation of the lower esophagus over the telephone in conversation with the surgical resident, on the basis of subcutaneous emphysema in a patient who had upper abdominal pain, no dyspnea or cough. The roentgenogram, as I have indicated, is, however, a much earlier and a better determinant of the presence of air in the para-esophageal interstitial tissues.

I would like to cite an unfortunate happening attending operative closure of a cervical perforation of the esophagus which occurred after esophagoscopy, in the interest of those who may be disposed to try something of the sort. At the time of operation, the thought occurred to me that if the carotid sheath were opened and the smooth inner surface of that sheath sutured over the site of suture of the perforation, the risk of mediastinitis would be lessened. The patient was maintained in the Trendelenburg posture and no mediastinal abscess developed. The patient's convalescence seemed assured, and somewhat more than a week later, I withdrew a soft rubber tissue drain (Penrose) which had been left in the wound. A slight blood stain was noted on the dressing subsequently, but a few hours later the patient died suddenly from profuse bleeding from the wound. I had anticipated finding the source of hemorrhage in an intervertebral vein or from the left internal jugular at postmortem. Much to my astonishment and amazement, however, the erosion was in the common carotid artery. Whereas, the use of the carotid sheath may secure the esophageal suture line, it is decidedly not a safe procedure.

This experience leads me to make a brief digression. It seems a bit odd that the thick walled artery should have ruptured rather than one of the adjacent thin walled veins. It seems to me that this very occurrence sheds some light upon the shortness of our years. Our arteries are called upon to sustain a relatively great pressure unrelentingly over years. Is it not likely that arteriosclerosis may be largely a traumatic process? If it is metabolic in origin, why do not veins exhibit these age changes in the same measure as it is observed in arteries? It may well be that the biblical three score and ten years are determined by the length of time that arteries will withstand the effects of systolic blood pressure.

I have had a single experience with an esophageal fistula resulting from pressure by a mediastinal abscess. What astounded me most about it was the great difficulty in securing closure of the fistula. After the performance of gastrostomy, I waited months for it to close spontaneously, no esophageal obstruction could be demonstrated. Yet this fistula stayed open until a very extensive decostalization, performed in stages, closed eventually both a total empyema and the esophageal fistula.

DR HERMAN E PEARSE (closing) Doctor Churchill has brought up the matter of after-care, particularly in relation to the feeding of patients with esophageal lesions. This is very important, for fluid balance must be maintained, blood is often needed, not only to supply hemoglobin but also deficient serum protein and oxygen may be required for prolonged periods in a tent

Feeding may be difficult. I have had a discouraging experience with the duodenal tube, largely because the patient is already uncomfortable from the wound, the manipulation of the oxygen tent, and the administration of fluids. I have tried it repeatedly and have now returned to a gastrostomy as the simplest procedure.

I would agree entirely with Doctors Churchill's and Alexander's presentation that these patients must be individualized, and if I may be allowed to predict, I believe that with more experience, we will divide them into three groups. One will constitute those infections which slowly gravitate down fascial planes from the neck. They should be simply opened and drained. Nature's barrier against the spread of infection should not be broken down. In the next group are those who have either a spreading infection or a localized abscess below the level of the fifth or sixth dorsal vertebra. They certainly should be attacked through the chest wall. The fascial spaces from the neck extend only to the level of the sixth vertebra, so one cannot use the cervical incision for those at the lower level. The same approach should be used for long-standing abscesses in any location, for they need some collapsing of the chest wall in order to obliterate the cavity.

The third group are those described who have a virulent spreading supuration from a visceral perforation. Their treatment must be much more energetic than for a localized abscess, and if the perforation is above the sixth dorsal vertebra, the mediastinum should be drained immediately through the neck.

I have never encountered the complication of hemorrhage spoken of by Doctors Alexander and Wangenstein. We all know that Doctor Halsted devised a very ingenious method for the gradual occlusion of great vessels with an aluminum band. He stated that he had cured aneurysms but some patients died of hemorrhage, therefore, it has long been known that gradual pressure on a pulsating vessel will wear away its wall.

Two factors might increase the risk of hemorrhage. One is the dissection of the carotid artery to expose its wall in the incision. This is not necessary. It should be left alone with its fascial envelope intact. The second is the use of a hard drainage tube. In any experience I have had in operative vascular surgery, I have never seen soft material erode a vessel wall.

THE MANAGEMENT OF CERTAIN LESIONS OF THE ESOPHAGUS

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LESIONS of the esophagus resulting from foreign bodies, diverticula, lye burns, spontaneous rupture and ruptures resulting from direct violence are not common, when one considers how few cases of this type are seen when compared with other surgical lesions of the gastro-intestinal tract. A large percentage of the cases classified in this group are not seen by the surgeon early in the life of the lesion or injury, and when the surgeon is called, it is often after some complication has developed.

Today, the management of these lesions is well standardized after the contributions made by Jackson,² Judd,⁸ Lahey,⁴ Pearse,³ Shallow,⁷ Truesdale¹ and others. There may be some difference of opinion as regards the one or two stage operation, where esophagotomy is necessary. The two stage operation advocated by Judd and Lahey is generally considered the safest procedure and has been practiced in the cases to be presented in this paper.

The resultant danger from perforation of the esophagus, regardless of the location, becomes a serious complication. Rupture in the thoracic portion develops contamination of the mediastinal structures and a virulent infection, with few patients able to survive, in spite of surgical drainage. The mediastinitis following cervical perforation as described by Pearse is an indirect effect. The explanation of Pearse and others is that it results from a dependent spread of infection from the neck into the chest along the fascial spaces. There is abundant evidence to prove that a direct communication exists between the cervical region and the mediastinum. This is due to the fact that, during embryologic development, the mediastinal structures originate in the neck and migrate into the chest, carrying their enveloping fascia with them. The conception that the mediastinum begins at the diaphragm and ends at the base of the skull is logical since at no place is there a transverse demarcation to segregate these regions. This anatomic relationship emphasizes the need for protection against a spread of infection from the cervical region to the mediastinum, when dealing with lesions involving the cervical region of the esophagus requiring esophagotomy.

The addition of esophagoscopy, as practiced by the skilled endoscopist, has contributed to the diagnosis and management of this type of case. The close cooperation of the endoscopist, roentgenologist and surgeon is essential in the successful appreciation of the problems involved and the ultimate result.

A foreign body lodging in the esophagus, or a lesion resulting from a foreign body, is the one most frequently seen by the endoscopist. The refinement of technic as practiced today fortunately minimizes the need for open operation. The work of Chevalier Jackson and his associates stands

out preeminently in the development of an excellent operative technic, which has resulted in a surprisingly low mortality of 2 per cent or less. He regards the esophagoscope, in the hands of rough, careless, unskilled physicians, as a dangerous and often fatal instrument. Moreover, there are risks associated with the use of the esophagoscope which he describes as "complications and dangers." Jackson has stated that "endoscopic skill cannot be bought with instruments. Repeated exercise of a particular series of maneuvers is necessary. As with learning to play a musical instrument, a fundamental knowledge of technic, positions, and landmarks is necessary, after which only continued manual practice makes for proficiency."

The management of pulsion esophageal diverticula, as described by Lahey, shows a refinement in technic, with gratifying results as shown in his follow-up of the cases operated upon. He has emphasized the need for early recognition of this lesion and surgical treatment, preferring the two stage operation, at the same time recognizing the results obtained by the advocates of the one stage operative procedure.

The great majority of cicatricial stenoses of the esophagus are seen in children as a result of the accidental swallowing of lye. When these cases are first seen, they should be treated conservatively, allowing only bland fluids for a period of about two weeks. The resultant strictures of the esophagus are often multiple, and may be resistant to treatment. Early dilatation of strictures of the esophagus has been practiced by Salzer and Bokay with satisfactory results. Most observers prefer waiting until the acute inflammatory reaction has subsided.

Where no gastrostomy is performed, we believe Jackson's peroral esophagoscopic bouginage for cicatricial stenosis, under direct vision, is safe and produces good results. Blind bouginage is to be strongly condemned. Where dilatation from above is impossible, the surgeon is called upon to perform a gastrostomy, not only for feeding purposes, but for future retrograde dilatation. Tucker claims this the safest method, and the results are more permanent and more rapidly attained. The Stamm type of gastrostomy has been found satisfactory, precaution being taken to select the site near the cardia, midway between the greater and lesser curvatures of the stomach.

The following case reports illustrate some of the problems encountered and the management of certain surgical lesions of the esophagus.

FOREIGN BODIES

Case 1—J. C., white, male, age 3, was admitted to the hospital March 2, 1936, with a history of having swallowed an alarm clock key that day. The child soon coughed and choked. He was referred to the endoscopist and later fluoroscoped, the key being found at the level of the fifth cervical vertebra (Fig. 1).

Esophagoscopy was carried out by Dr. H. Lee Simpson, who visualized the foreign body below the level of the cricoid. It was so tightly incarcerated and fixed that it could not be turned, removal by this route, therefore, was considered impossible. The following day, March 3, 1936, a first stage external esophagotomy was performed.

Operation—The esophagus was exposed, two long black silk sutures were inserted into the wall for subsequent identification, and the wound packed. The patient was given

intravenous glucose and saline subcutaneously for the next few days. On March 8, 1936, the second stage esophogotomy was performed under general anesthesia. The foreign body could not be felt, but a roentgenogram showed it to be at the level of the fourth cervical vertebra. A one-half inch incision was made in the esophagus, and with the aid of a Cameron light, the foreign body was seen, grasped with a forceps, and gently removed, under vision. The defect in the esophagus was closed by interrupted catgut sutures. The wound was closed in layers, with a small rubber drain inserted at the lower angle. A Levine tube was passed for feeding purposes and removed 11 days later.

Subsequent Course—There was no noticeable drainage from the wound. The patient was discharged 20 days postoperatively. One month later, he was reported to be in good condition.



FIG 1—Roentgenogram showing an alarm clock key in the esophagus at the level of the fifth cervical vertebra.



FIG 2—Roentgenogram showing a razor guard in the esophagus at the level of the transverse arch of the aorta.

Case 2—T. D., white, male, age 46, was admitted to the hospital December 12, 1934, with a history of having been in an institution during the previous five months because of a mental condition. One month prior to admission to Harper Hospital, he had attempted suicide by swallowing the two parts of a safety razor which hold the blade. One piece was reported as having been passed per rectum. Following the swallowing of the safety razor guard, he had intermittent attacks of severe substernal pain. Fluoroscopic examination revealed a metallic guard from a safety razor in the lower esophagus, about four inches above the cardiac end. Temperature, 102° F, pulse, 100, respirations, 24. *Physical Examination* did not reveal any evidence of cyanosis, or emphysema of the soft tissue of the neck and thorax. The following day, he was esophagoscoped by Dr. A. E. Hammond. A 9 Mm esophagoscope was passed, and about three inches above the diaphragm, the esophagus was observed to be studded with granulation tissue, which was partially removed, and the metal foreign body visualized. This was grasped with a heavy, forward-grasping forceps, and gently pulled upward. It was brought to the level of the cricoid cartilage, at which point it was impossible to pull it further. The following day, roentgenologic examination of the chest, in the anteroposterior and lateral planes, revealed the safety razor guard lying at the level of the transverse arch of the

aorta (Fig 2) At this time, there was no evidence of emphysema, and both lung fields were normally aerated

A roentgenologic examination of the chest four days later showed the guard to have descended about two inches since the former examination The patient was again esophagoscoped, December 19, 1934, and a 9 Mm esophagoscope was passed With the Toddle forceps, the operator was able to grasp the foreign body and it was elevated to the level of the cricoid cartilage, but again it was found impossible to extricate it further On December 23, 1934, it was decided that the foreign body should be removed by the external route

Operation—December 26, 1934 The first stage operation was performed, which simply exposed the esophagus A gauze pack was inserted down to the esophagus, and the wound closed Convalescence was uneventful, and five days later the second stage operation was performed The esophagus was exposed, and a one-half inch incision was made through its lateral aspect A short esophagoscope was then introduced, orally, and the foreign body was elevated to the level of the surgical incision in the esophagus, through which it was extracted The wound in the esophagus was closed, and a small soft rubber drain inserted A Levine tube was passed for feeding purposes Convalescence was uneventful, except for a small amount of drainage from the operative wound, and there was no evidence of an esophageal fistula The Levine tube was removed at the end of 12 days The surgical incision was completely healed January 16, 1935, at which time the patient was discharged from the hospital

Follow-Up—The patient has been seen on a number of occasions and has returned to his former occupation A fluoroscopic and roentgenologic examination with a barium meal, five weeks after operation, showed the barium to have passed through the esophagus without any evidence of obstruction, but there was present a moderate amount of spasm (Fig 3) There is no difficulty in swallowing, no evidence of stricture, and he is apparently normal mentally

Case 3—A P, white, female, age 44, married, entered the hospital April 21, 1937, with a history of having swallowed a fish bone a few hours previously Roentgenologic examination revealed the presence of a small bone in the esophagus at the level of the sixth and seventh cervical vertebrae It was also noted that there was some increased radiotransparency about the bone, suggesting the probability of some air in the peri-esophageal tissues The patient was esophagoscoped by Dr Arthur E Hammond, who visualized the fish bone lying cross-wise in the cervical region of the esophagus It was impossible to extract it with fine, grasping-forceps The patient was, therefore, returned to the ward, and fluids administered by both intravenous and subcutaneous routes Two days later, the patient's general condition appeared critical Temperature, 101° F, pulse, 108, respirations, 22 There was also noted a moderate cyanosis of the face, upper thorax and neck, pitting edema in both upper and lower extremities, and clinical evidence of emphysema in both cervical regions, which extended to the level of the clavicle on the left side Because of the cyanosis and dyspnea, the patient was placed in an oxygen tent, and treatment instituted to restore her fluid balance in preparation for the

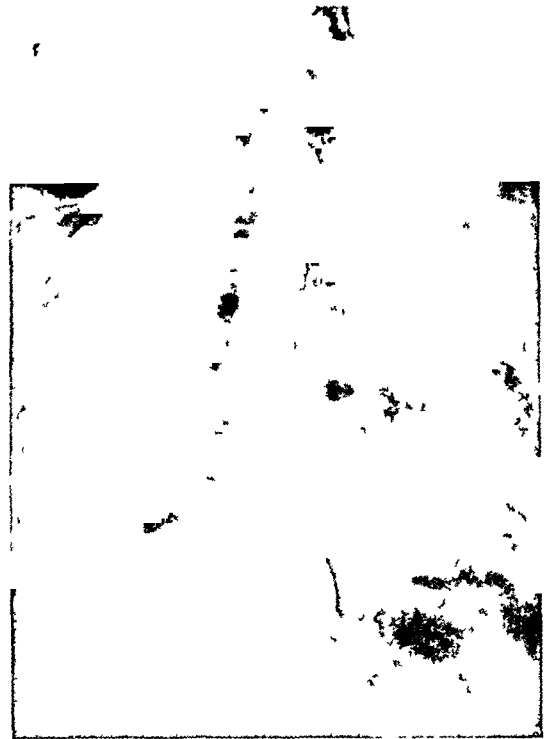


FIG 3—Roentgenogram taken six weeks after the removal of the foreign body by the external route There is no evidence of stricture but a moderate degree of spasm

first stage external esophagotomy A periesophageal abscess was suspected as being secondary to a perforation of the cervical esophagus

Operation—April 24, 1937, three days after admission A left, first stage external esophagotomy was performed under nitrous oxide anesthesia Upon exposing the esophagus at the level of the foreign body, there was found a walled-off abscess at the postero-lateral aspect of the esophagus (Fig 4A)

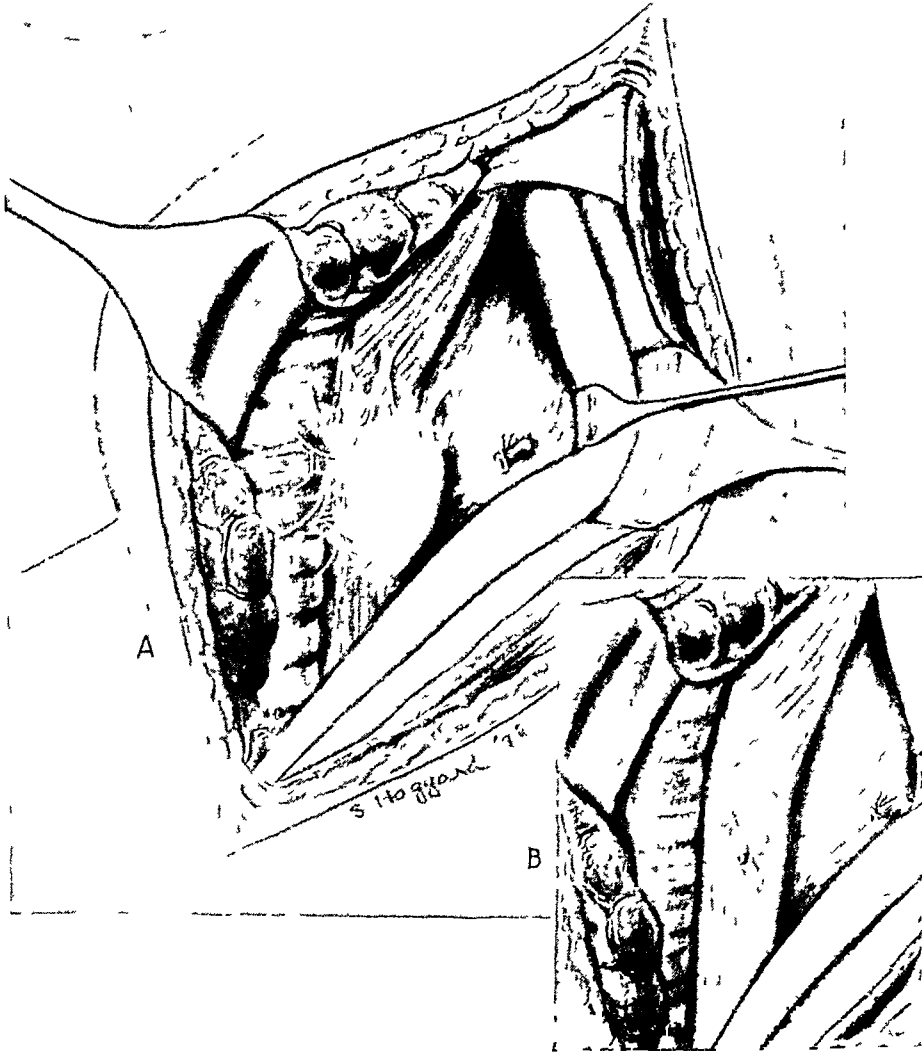


FIG 4—(A) Drawing of the periesophageal abscess found at operation (B) The small perforation in the wall of the esophagus which was seen after drainage of the periesophageal abscess

The wound was packed anteriorly, inferiorly and posteriorly, and the abscess drained. The culture of the pus was reported as *Staphylococcus aureus*. At this operation, a small perforation in the wall of the esophagus was seen (Fig 4B). A small rubber drain was inserted to the site of the perforation and placed in the lower angle of the wound. The patient's postoperative condition was satisfactory, and the fluid requirements were met by glucose intravenously and saline subcutaneously. There was a small amount of drainage of a serosanguineous type from the wound during the next few days. Roentgenologic examination, April 28, 1937, revealed no definite evidence of the fish bone shadow in the cervical region. At this time the patient was esophagoscoped by Doctor Hammond, who reported the cervical portion of the esophagus to be slightly inflamed and after careful inspection, found no tear in the esophageal wall, or foreign body. The

ESOPHAGEAL LESIONS

esophagoscope was passed gently down to the cardia. It was concluded that the foreign body had passed down into the gastro-intestinal tract. A Levine tube was passed for feeding purposes, and was removed May 4, 1937, when fluids were given by mouth. There was apparent need for maintaining drainage for 11 days, at the end of which time the temperature, pulse and respirations were normal, and the patient was discharged. Recovery was uneventful. At the present time, the patient is reported in good health and has had no symptoms referable to the esophagus.

ESOPHAGEAL DIVERTICULUM

Case Report—H. A., white, male, age 60, first came under observation October 19, 1932, with a history of having had difficulty in swallowing for two years. This difficulty had been progressive in type, and was not associated with any hoarseness. He stated that a fulness in the lower left neck region appeared usually after his evening meal. Three or four hours later, by exerting pressure over this area of fulness, he was able to express previously eaten food into the mouth. At this time, the patient was not acutely ill and weighed 121 pounds. Examination showed a slight fulness in the neck in the region of the left lobe of the thyroid. He was referred for roentgenologic study October 24, 1932. Fluoroscopic examination demonstrated a very definite distention of the upper third of the esophagus, with a large diverticulum bulging from the posterior aspect of the esophagus just at the suprasternal notch (Fig. 5). The barium trickled through the esophagus below this point, and there was no indication of any other abnormality.

Operation—October 28, 1932. A first stage external esophagotomy was performed under bilateral paravertebral-cervical nerve block anesthesia. The left lobe of the thyroid was mobilized and retracted to the midline, exposing the diverticulum. The latter was freed along its entire length down to its communication with the esophagus. The sac was anchored to the prethyroid muscle, iodoform gauze was packed around the diverticulum and was brought out through the lower end of the wound. A Levine tube was passed for feeding purposes. Convalescence, after the first stage operation, was uneventful, except for a small amount of seromucous drainage from the wound. There was apparently a small tear made in the wall of the diverticulum at the time of its isolation, resulting in a small esophageal fistula. On November 16, 1932, 18 days later, the second stage operation was performed. The sac was excised, and the small defect in the esophagus was closed. The patient was fed by a Levine tube until November 20, 1932, when the tube was removed and fluids allowed by mouth. The drains were removed from the wound November 21, 1932, and the patient was discharged. When last seen, in the spring of 1937, the patient reported no difficulty in swallowing, and was in good general health except for a mild hypertension.

CONGENITAL SHORTENING OF THE ESOPHAGUS

Case Report—L. S., male, age seven weeks, was admitted March 29, 1933, with a history of vomiting after taking his formula from the time he was one week old. The vomiting occurred one-half to two hours after the feedings, and occasionally was projectile in type. The vomiting continued and fluoroscopic and roentgenologic studies were made April 3, 1933, and April 23, 1933, which demonstrated a congenitally short esophagus and a pouch-like projection of the stomach above the diaphragm (Fig. 6).

From the clinical and roentgenologic findings, it was decided to perform a left phrenic crushing procedure, which was effected April 29, 1933. All vomiting ceased thereafter, and the child has had no further difficulty.

STRICTURE OF THE ESOPHAGUS

Case Report—L. G., colored, female, age 3, was admitted to the Children's Hospital June 12, 1935, with a history of having swallowed lye about ten weeks previously. Since then, she had considerable difficulty in swallowing. A diagnosis was made of an esophageal stricture secondary to a lye burn. Roentgenologic examination demonstrated the presence of a complete stricture of the lower third of the esophagus (Fig. 7).



FIG 5—Roentgenogram showing an esophageal diverticulum measuring 4 cm in diameter



FIG 6—Roentgenogram showing the short esophagus and a portion of the stomach lying above the diaphragm. There is also to be noted a distinct dilatation of the esophagus and a pouch like projection from both aspects of the stomach above the diaphragm

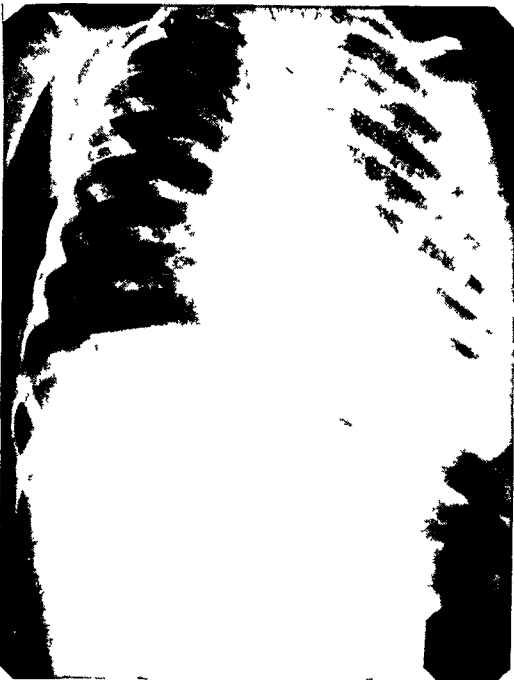


FIG 7—Roentgenogram taken approximately ten weeks after a lye burn, demonstrating practically a complete stricture of the lower third of the esophagus. There is considerable dilatation of the esophagus above the stricture



FIG 8—Roentgenogram (lateral view) of the esophagus 34 months after treatment

The child was discharged without treatment, but was readmitted one month later, during which interval she had lost 12 pounds in weight. At the time of readmission, she was able to take only fluids by mouth. July 30, 1935, a 6 Mm esophagoscope was passed by Drs. A. E. Hammond and Wadsworth Warren. Just below the area of the cricopharyngeus there was a marked stricture. A No. 10 esophageal bougie was introduced, and the stricture dilated. Three months later, a 6 Mm esophagoscope was again passed by Doctors Hammond and Warren, down below the cricoid to the upper esophageal stricture. It was impossible to get through the stricture further than about one-half inch with the smallest esophageal bougie available.

A gastrostomy was deemed advisable and the Stamm type of operation was performed October 30, 1935. On November 12, 1935, a 6 Mm esophagoscope was passed down to the upper stricture. This was dilated with some difficulty by a No. 10 French bougie. Gradually the esophagoscope, together with the bougie, was passed down through to the lower esophagus. The No. 10 French bougie was then withdrawn, with the string positor, and the bougie was passed through into the stomach. With the aid of the esophagoscope in the stomach, the string was grasped and brought out through the abdominal opening. A heavy silk cord was then tied and withdrawn through the esophagus, inserted through the nares, and the loop completed. A week later, the esophagus was dilated, using a retrograde Tucker French No. 12 bougie. Some resistance was encountered. After four months (March 31, 1936) it was possible to dilate with a No. 20 French bougie, dilatation having been performed every two weeks. On July 21, 1936, it was possible to pass a No. 24 French bougie, and on September 15, 1936, retrograde esophageal dilatation with a Tucker No. 30 French bougie was accomplished. During 1937, the patient was dilated with a Tucker No. 30 French bougie every month, with no difficulty. At the time of the dilatation, November, 1937, she was told to return in three months. On April 19, 1938, a retrograde Tucker No. 30 French bougie was passed without difficulty (Fig. 8). It is planned at this time to close the gastrostomy, inasmuch as the patient has been taking solid food for the past year with no evidence of contracture of the former stricture.

RUPTURE OF THE THORACIC ESOPHAGUS

Case Report—C. B., white, male, age 2, was admitted to the hospital August 6, 1935, with a history of having been well until July 30, 1935. The swallowing of a foreign body on that date was suspected. It was reported that previous to admission to the hospital, the child had eaten very little, and had vomited repeatedly since the onset of symptoms.

Physical Examination revealed a well nourished child, appearing dehydrated. Temperature, normal, pulse, 110, respirations, 24. The fontanelles were closed, pupils, equal, and reacted to light, ears and nose, negative, tongue, dry, and the throat, slightly injected, but no foreign body was seen. There was no rigidity of the neck, but on examination of the chest, an occasional coarse râle was heard over both bases. The heart borders were normal, and no murmurs were heard. The abdomen was soft, liver and spleen not palpable. A diagnosis of suspected foreign body in the esophagus was made. On August 7, 1935, the patient was esophagoscoped by Dr. A. E. Hammond, who found no evidence of a foreign body in the esophagus, but did see an ulcer approximately 1.1 cm in the left lateral wall, about one inch above the cardia. The floor of the ulcer was necrotic and surrounded by a zone of hyperemia. After this examination, the child strained considerably and vomited. Approximately four hours later, there were signs of a left tension pneumothorax, which was aspirated, 400 cc of air and 20 cc of sero-sanguineous fluid being removed, with marked relief of the dyspnea. This finding of tension pneumothorax with fluid in the pleural cavity led us to suspect that the esophageal ulcer had perforated into the left pleural cavity.

Fluoroscopic examination, at 9:00 P.M., revealed that there was a total collapse of the left upper lobe, and a 50 per cent collapse of the left lower lobe, with marked displacement of the heart to the right. The child was placed in an oxygen tent with no

apparent improvement. Because of the increase in the severity of the tension pneumothorax and the inability to control it by aspiration, it was deemed advisable, at 11 00 P M, to institute a closed catheter type of drainage under water. This resulted in marked relief of the dyspnea and cyanosis. Unknowingly, a student nurse gave the child milk to drink, and immediately the milk appeared in the drainage tube which had been placed in the left pleural cavity. This definitely proved that there was a perforation of the esophagus into the left pleural cavity. A Levine tube was inserted into the stomach for feeding purposes, putting the esophagus at rest. Fluoroscopic examination and roentgenologic examination, August 8, 1935, showed the drainage tube in the left pleural space, with no indication of free air or fluid in the left pleural cavity. The rectal temperature varied from 102° to 104° F for two days following the rupture of the esophagus.

Roentgenologic examination, August 15, 1935, revealed the lung almost completely reexpanded. The Levine tube was used for feeding purposes until August 20, 1935, when fluids were given by mouth. The fluid which drained through the catheter showed no growth on culture. The tube was removed from the pleural cavity on August 26, 1935, and the child was discharged four days later.

Subsequent Course—Fluoroscopic study, September 30, 1935, after a barium meal, showed that there was no interruption in the downward progress of the barium into the stomach. The lumen of the esophagus was reported small, but there was no abnormality in the contour of this structure at the site of the previously reported rupture. May 24, 1937, 21 months after the rupture, there were no symptoms referable to the esophagus or thoracic organs. Fluoroscopic examination after the administration of barium revealed no evidence of obstruction or stricture in the esophagus.

CONCLUSIONS

(1) Various lesions of the esophagus coming to the attention of the surgeon have been briefly discussed and cases illustrating their management have been described.

(2) The management of lesions of the esophagus requires close cooperation between the endoscopist, roentgenologist and surgeon.

(3) The two stage procedure of esophagotomy carries a low mortality rate if performed at the optimum period.

(4) Strictures of the esophagus demand careful treatment over an extended period in order to obtain satisfactory end-results.

(5) Rupture of the thoracic esophagus demands early diagnosis and drainage of the pleural cavity.

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LYMPHATIC SPREAD OF CARCINOMA OF THE RECTUM

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CHICAGO, ILL

THE OPERABILITY and prognosis in patients with carcinoma of the rectum depend on the presence and extent of lymphatic metastases as well as on the degree of local extension of the tumor and the absence of blood-borne metastases to the liver, lungs, bones, brain, *etc* The present study was undertaken in an effort to determine the incidence, extent and location of lymph node metastases and the extent of radical removal necessary to insure eradication of all involved nodes

At first, this was done by a very careful dissection of the fresh, surgically removed specimen of carcinoma of the rectum A full scale drawing was made, and the location of all lymph nodes was carefully noted on it Between eight and 48 lymph nodes were found in each of 22 specimens examined by gross dissection Nodes which were thought to be involved with carcinoma were labeled and circled with black ink on the drawing All nodes were then sectioned and examined microscopically

Recognition of involved nodes by palpation is difficult or impossible when they are small Four hundred ninety-six nodes from these specimens were examined grossly to determine the presence of metastases Of the 111 lymph nodes containing carcinoma, only 48 showed any gross change, even in cross-section of the gland Gabriel, Dukes and Bussey¹ tried to determine the presence of lymph node metastases in 1,242 nodes found in operative specimens of carcinoma of the rectum Of 337 nodes considered by them to have carcinoma grossly, only 132 were found to be involved when examined microscopically, and of 905 nodes considered to be free of carcinoma, 18 contained carcinoma when examined microscopically

Technic of Examination—Later, in order to more accurately study all of the lymph nodes, we developed the following technic for examination of surgically removed specimens of carcinoma of the rectum The ligature on the superior hemorrhoidal artery of the fresh specimen is removed and a small cannula is tied into the artery The specimen is then perfused with a warm 1 per cent citrate solution under a pressure of about 100 cm of water Ligatures on the smaller vessels are removed so that the blood can be washed out, and as soon as there is a free flow of clear fluid from any open vessel, it is ligated After one to three hours of perfusion, the specimen is white except for the extrinsic muscles surrounding the anal orifice, and for any small areas where there may have been an extravasation of blood Such areas can be cleared by very gentle manipulation After the specimen has become almost entirely white, the artery is injected with red lead This is done under moderate pressure, using a syringe The vessel is then tied and the specimen is

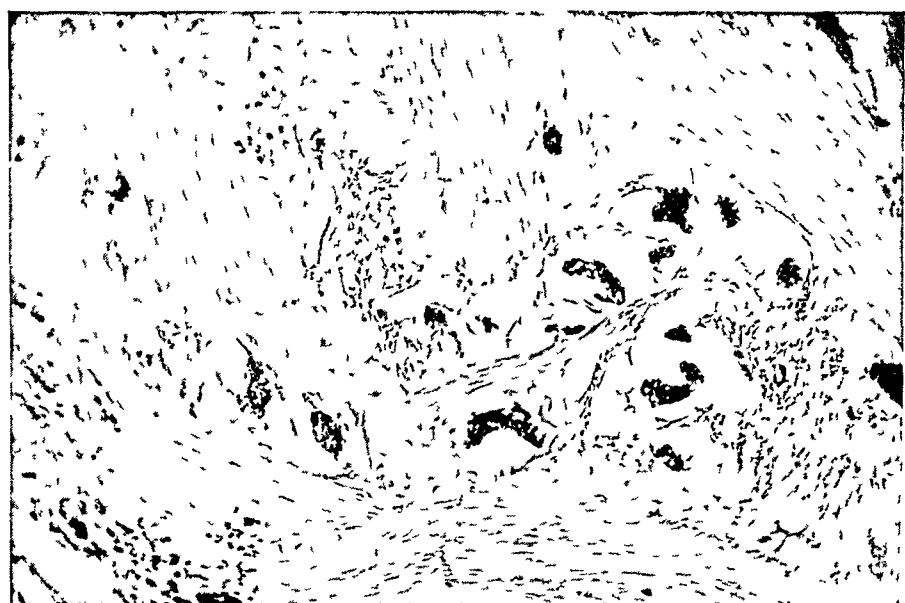
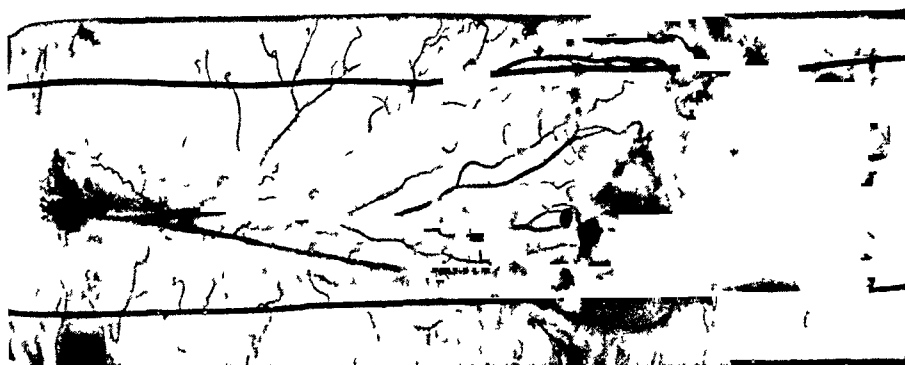
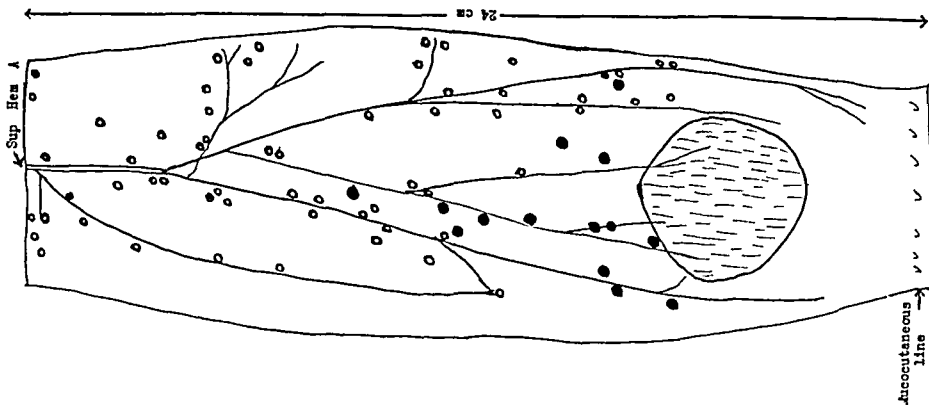


FIG. 1.—Hosp. No. 34300. Gross specimen and photomicrograph. A photograph of the cleared transparent preparation of this specimen shows the arterial tree as branching, black lines. The lymph nodes are represented by the spherical dark areas seen throughout the tissue. Those containing carcinoma are indicated by solid black dots. The normal lymph nodes are represented by hollow circles.

placed in 10 per cent formalin solution for 24 hours. It is then changed every 24 hours from 50 to 70 to 95 per cent to absolute alcohol. If the fascia propria is untorn or if the tumor is thick, it is better to leave the specimen in alcohol for a longer time. The bowel is then opened along the antimesenteric border. This preserves the arterial tree and allows for an accurate localization of the tumor and its regional nodes. The specimen will now be completely white. It is mounted on any suitable frame with a few silk sutures and placed in methyl salicylate. After 24 to 48 hours the specimen becomes almost completely transparent. The red arterial tree serves as a very good landmark. The tumor, mucosa and peritoneum can all be easily recognized and the lymph nodes stand out as spherical masses of a slightly greater density than the surrounding tissue. Many bubbles will be found. These can be expressed by gentle pressure. The tissue can be handled with ease and safety if left beneath the surface of the methyl salicylate. Sometimes it takes five to seven days for all bubbles within the depth of the tissue to disappear (Fig. 1).

A full scale drawing of the bowel, arterial tree and tumor is then made. A section of the tumor is taken and placed in methyl salicylate. The lymph nodes can now be removed, each one can be labeled separately and its position charted exactly in its relation to the artery. These nodes are then placed in methyl salicylate and they are ready to imbed in paraffin and section and stain without being run through the usual alcohol and xylol solutions.

Specimens studied in this way have had 20 to 80 nodes per specimen. The average in 25 transparent specimens removed by the Miles type of abdomino-perineal resection of the rectum was 52.1 nodes per specimen. Sixteen of the 22 specimens studied by gross dissection had lymph node metastases, and 16 of the 25 studied by the method of clearing had metastases, an average of 68.1 per cent of all specimens studied. Previous studies of lymph node involvement are summarized in Table I.

TABLE I

SUMMARY OF INCIDENCE OF LYMPH NODE INVOLVEMENT BY PREVIOUS AUTHORS

Author	Number of Specimens Studied	Number of Nodes per Specimen	Percentage with Metastases to Nodes
McVay, J. R. ²	100	6.23	47%
Wood, W. Q., and Wilkie, D. P. D. ³	100	11.23	51%
Westhus, H. ⁴	74 (cleared)	25.33	59%
Gabriel, W. B., Dukes, C., and Bussev, H. J. R. ¹	100	28	62%
Gilchrist, R. K., and David, V. C.	22 (gross)	23.9	68.1%
	25 (cleared)	52.1	

Dukes'¹ classification divides tumors into Grade A, where the tumor does not penetrate the bowel wall and does not have lymph node metastases, Grade B, where the tumor extends through the bowel wall and involves adjacent tissue but does not have lymph node metastases, and Grade C, where

there are metastases to lymph nodes. An analysis of the tumors studied in this series is given in Table II, which shows that tumors having lymph node

TABLE II

SUMMARY OF GRADINGS OF METASTASES ACCORDING TO THE CLASSIFICATIONS OF BRODERS AND DUKES

	32 Specimens With Metastases*	15 Specimens Without Metastases
Broders' Grades		
1	0	3
2	20	11
3	10	1
4	2	00
Dukes' Grades		
A	0	5
B	0	10
C	32	0
Number of involved nodes per specimen		
1	5	
2	5	
3	4	
Many	18	

* Specimens with metastases to high lying nodes, 19

metastases tend to be of a higher grade classification, according to Broders' grading, than those without metastases. Eighteen of the 32 specimens having metastases had four or more nodes per specimen involved. Nineteen of the 32 had node involvement at or above the bifurcation of the superior hemorrhoidal artery.

Tumors arising predominantly on the mesenteric border of the bowel seem to metastasize to the lymph nodes more frequently than do those arising on the antimesenteric border (Table III).

TABLE III

LOCATION OF TUMOR ON CIRCUMFERENCE OF THE BOWEL

	Mesenteric Border	Antimesenteric Border	Circular
32 specimens with metastases	17	12	3
15 specimens without metastases	7	7	1

The duration of symptoms seems to have less effect than one would suppose on the number of nodes involved in operable cases. Three patients who had had symptoms for four months or less had 22, 25 and 28 involved nodes, while five patients who had had symptoms 12 to 18 months had zero, two, three, two, and 43 involved nodes (Table IV).

CARCINOMA OF RECTUM

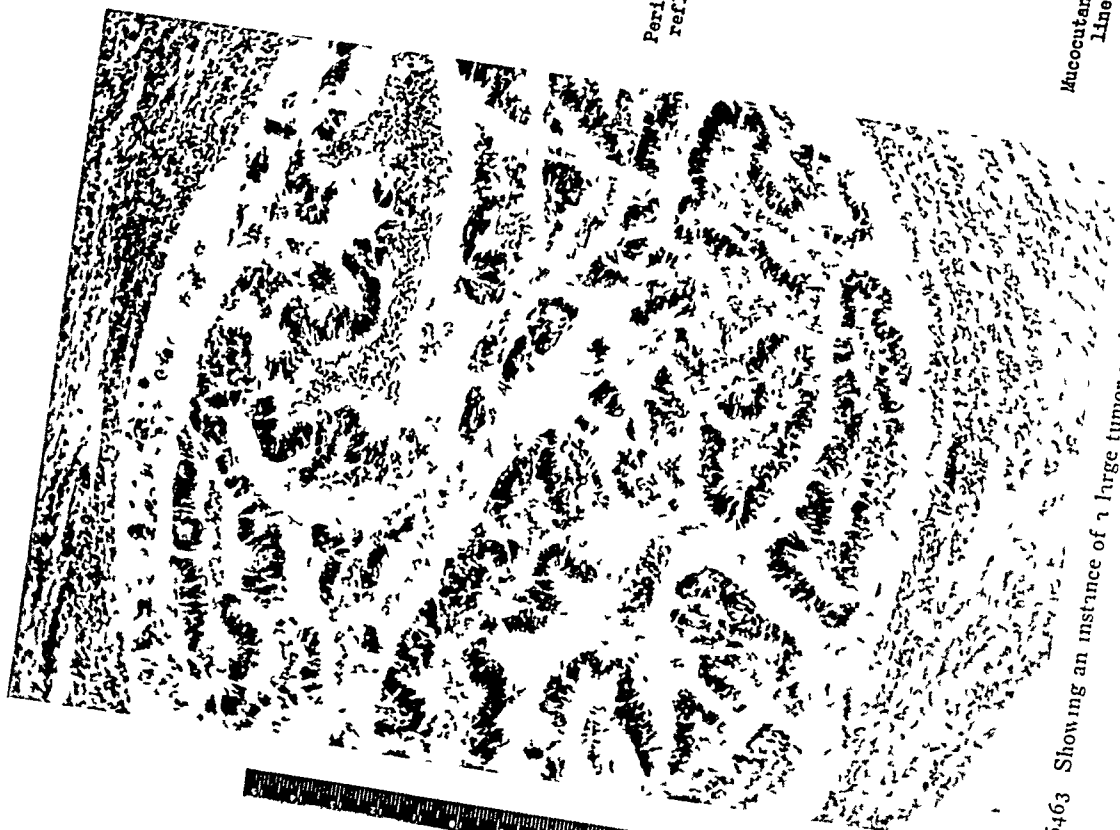
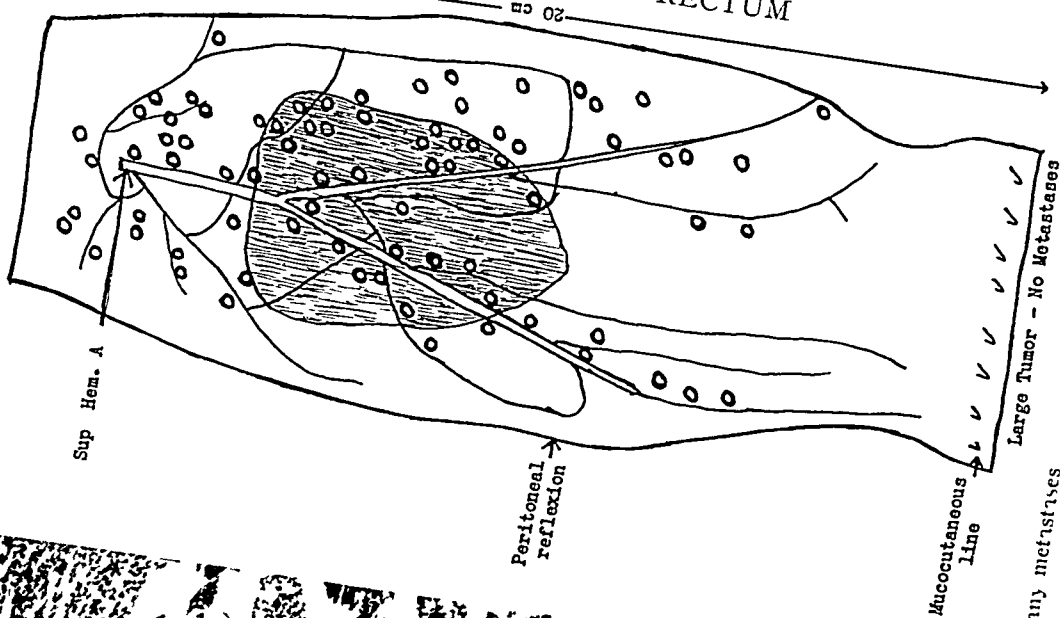
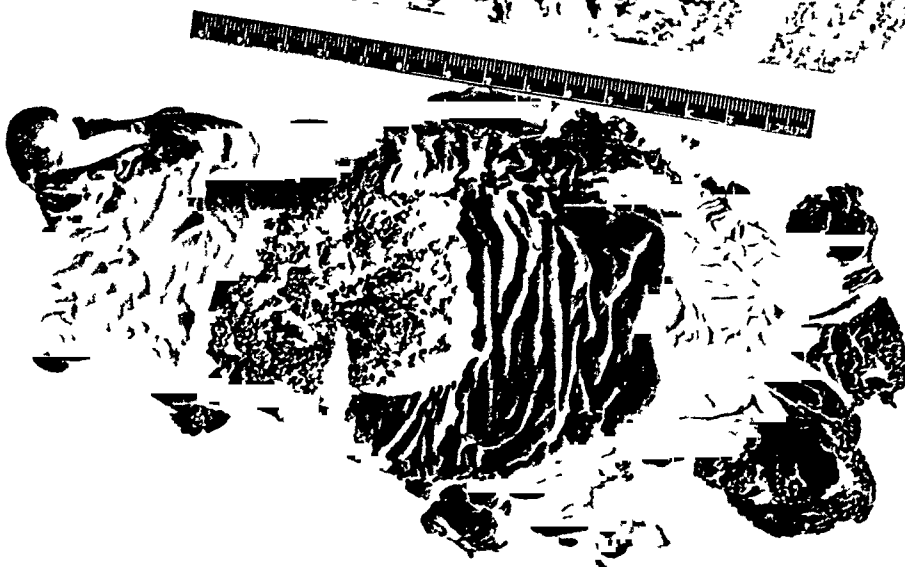


FIG 2—Hosp No 36463 Showing an instance of a large tumor without the occurrence of any metastases



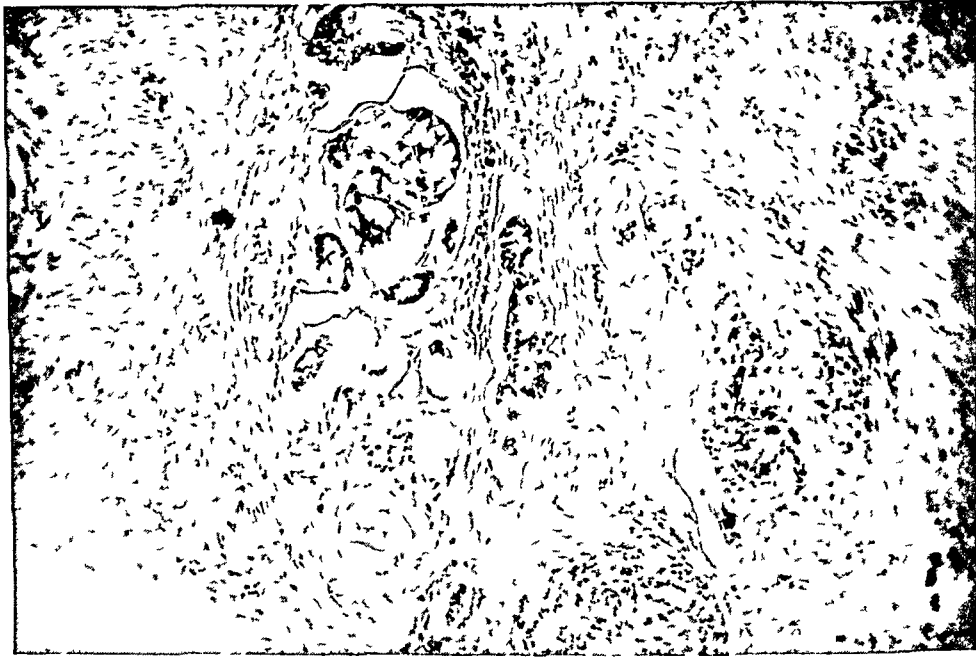
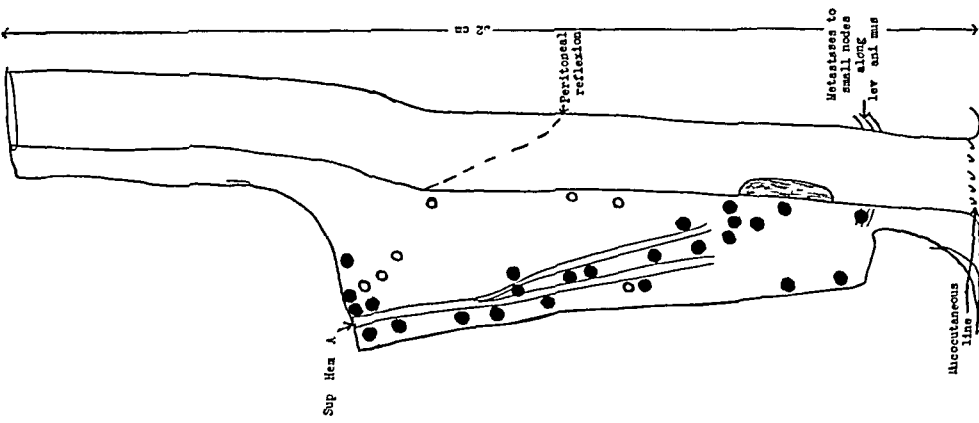
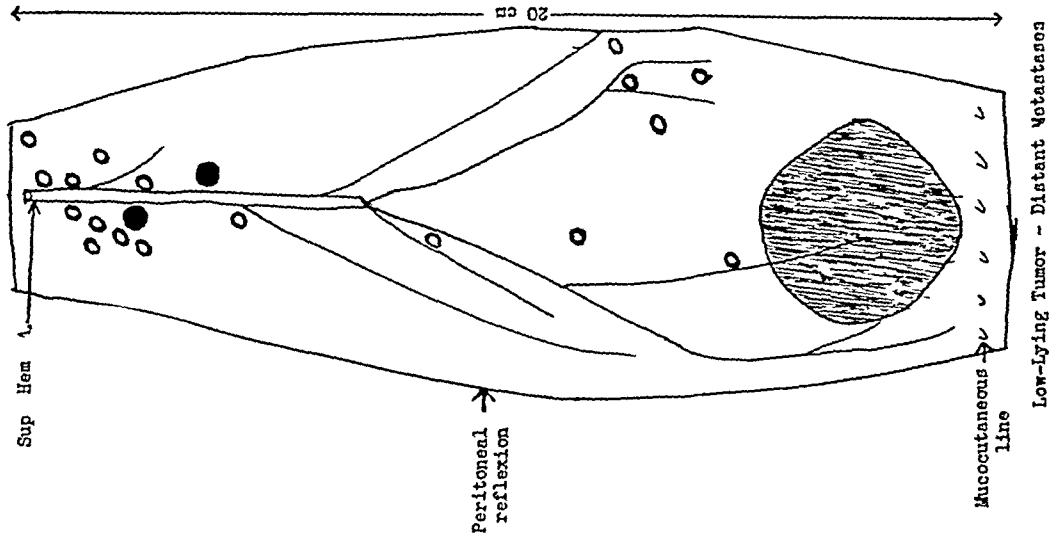


FIG 3—Hosp No 34434 Showing an instance of a small tumor with very extensive metastases



CARCINOMA OF RECTUM



Low-lying Tumor - Distant Metastases
Showing a low lying tumor with distant metastases, without any apparent intervening involvement



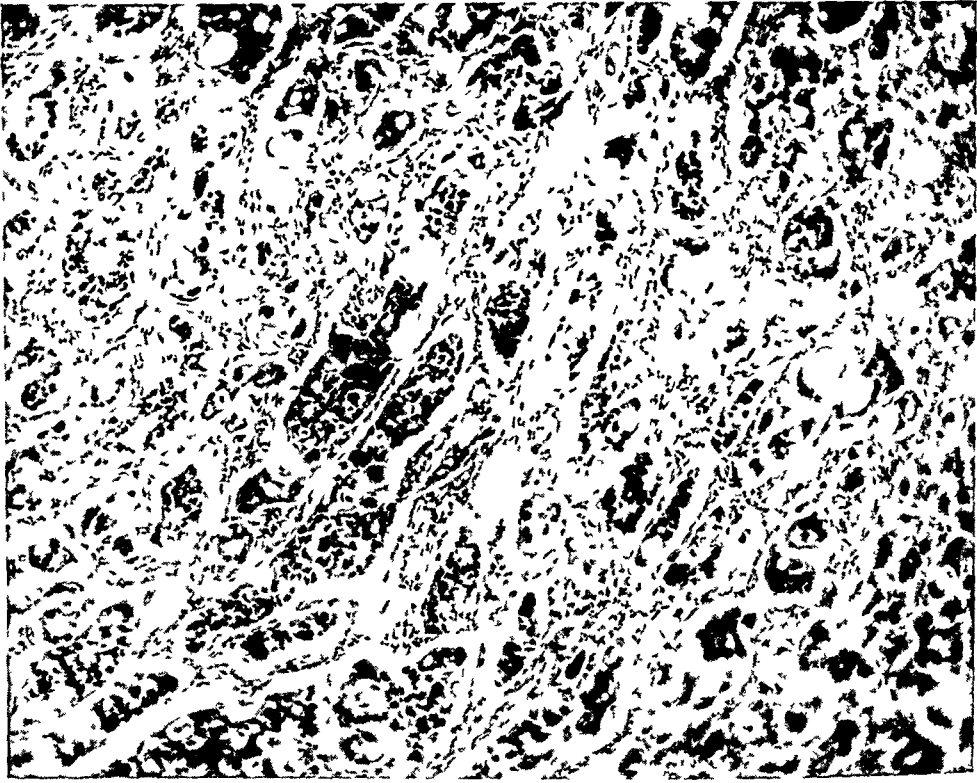
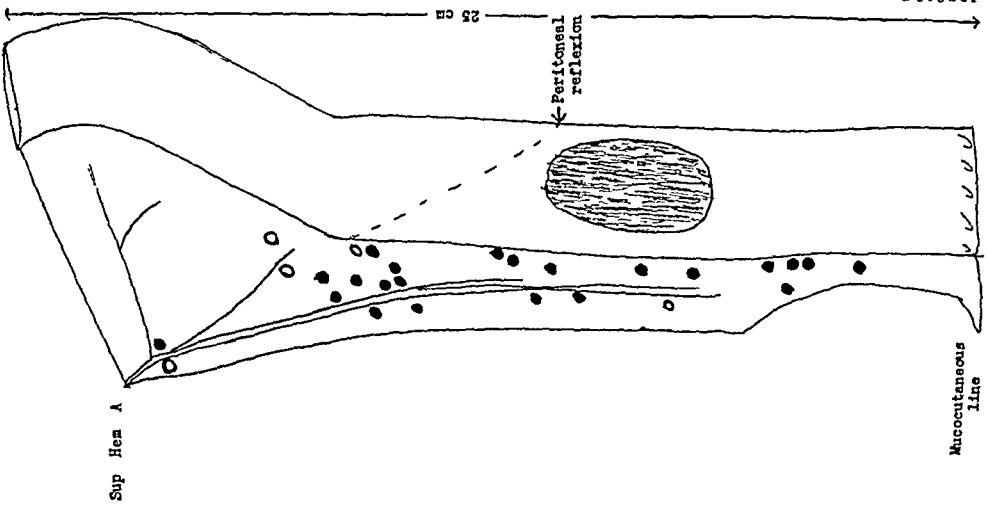


FIG 5.—Hosp No 33779 Showing an instance of retrograde metastases The lowest of the involved nodes being 4 cm below the inferior edge of the tumor

CARCINOMA OF RECTUM

TABLE IV

INCIDENCE OF METASTASES IN RELATION TO DURATION OF SYMPTOMS

Number of Nodes Involved per Specimen	Number of Cases with Symptoms 6 Months or Less	Number of Cases with Symptoms for More Than 6 Months
4 or more nodes	11	7
3 or less nodes	10	4
No nodes involved	6	9

The size of the tumor seems to have little relation to the number of nodes involved with metastases (Table V)

TABLE V

LYMPH NODE METASTASES IN RELATION TO THE AMOUNT OF CIRCUMFERENCE OF BOWEL INVOLVED

	More Than 75 Per Cent	Less Than 75 Per Cent
Specimens with 3 or less involved nodes	7	7
Specimens with 4 or more involved nodes	7	11
Specimens without metastases	8	7

Analysis of the specimens studied in this series has led us to the following conclusions

(1) The size of the tumor is of little value in determining the presence or absence of lymph node metastases. Figure 2 (No. 36463) is an excellent example of this phenomenon. The patient, age 60, had had symptoms for eight months. He was very obese, which made radical removal difficult. The tumor involved at least 75 per cent of the circumference of the bowel. Eighty lymph nodes were removed from this specimen, all were normal. In contrast, Figure 3 shows the specimen from a patient, age 49, who had had symptoms for two months. The tumor involved about 20 per cent of the circumference of the bowel. The specimen was studied by gross dissection, 32 nodes were found, 25 of them contained metastases. Sixteen of the 25 involved nodes showed pathologic changes on sectioning, before fixation. There was one node found at the level of the levator ani muscle which was involved.

(2) Low-lying tumors may have metastases very high. Figure 4 shows the specimen of a patient, age 43, who had had symptoms for 16 months. The tumor involved about 65 per cent of the circumference of the bowel. Twenty nodes were found and the two solid black dots indicate the location of the lymphatic metastases.

(3) Where the upward lymph channels are blocked by metastases, there may be a retrograde metastasis downward as shown in Figure 5. The patient, age 65, had had symptoms for at least six months. The tumor involved about 65 per cent of the circumference of her bowel. Twenty-seven nodes were found by gross dissection, 22 of them having metastases. The lowest of the five nodes below the tumor was 4 cm below the lowest edge of the tumor. One other case showed the same anatomic distribution.

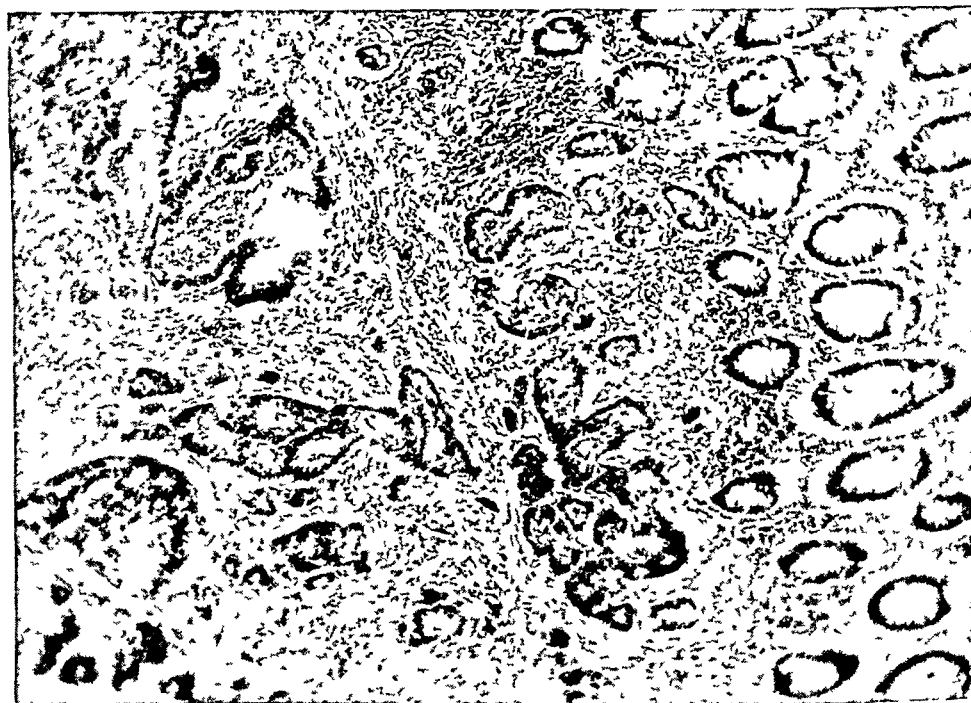
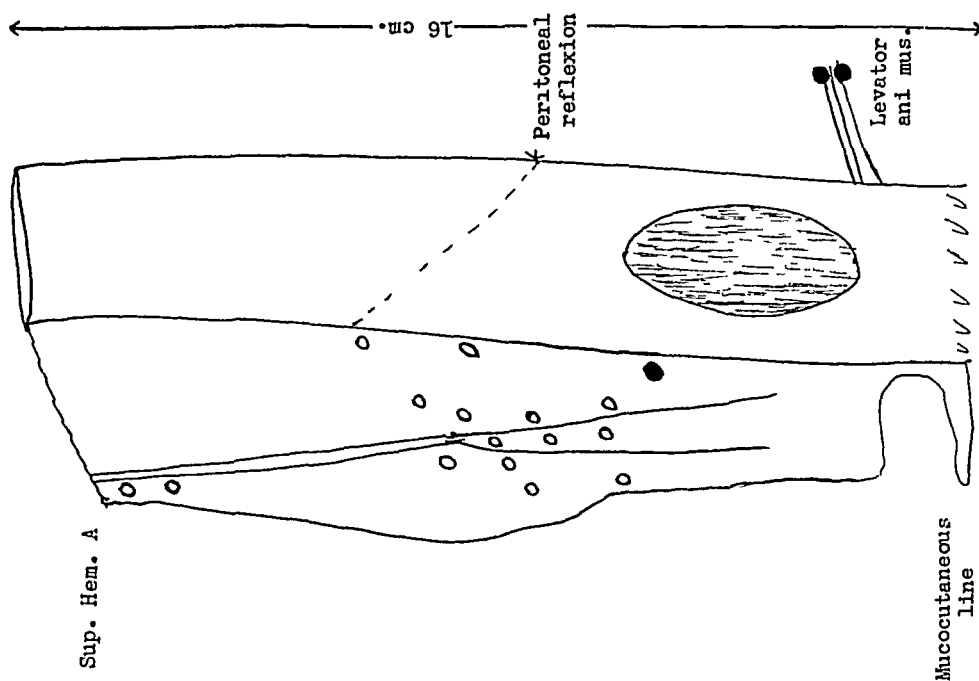
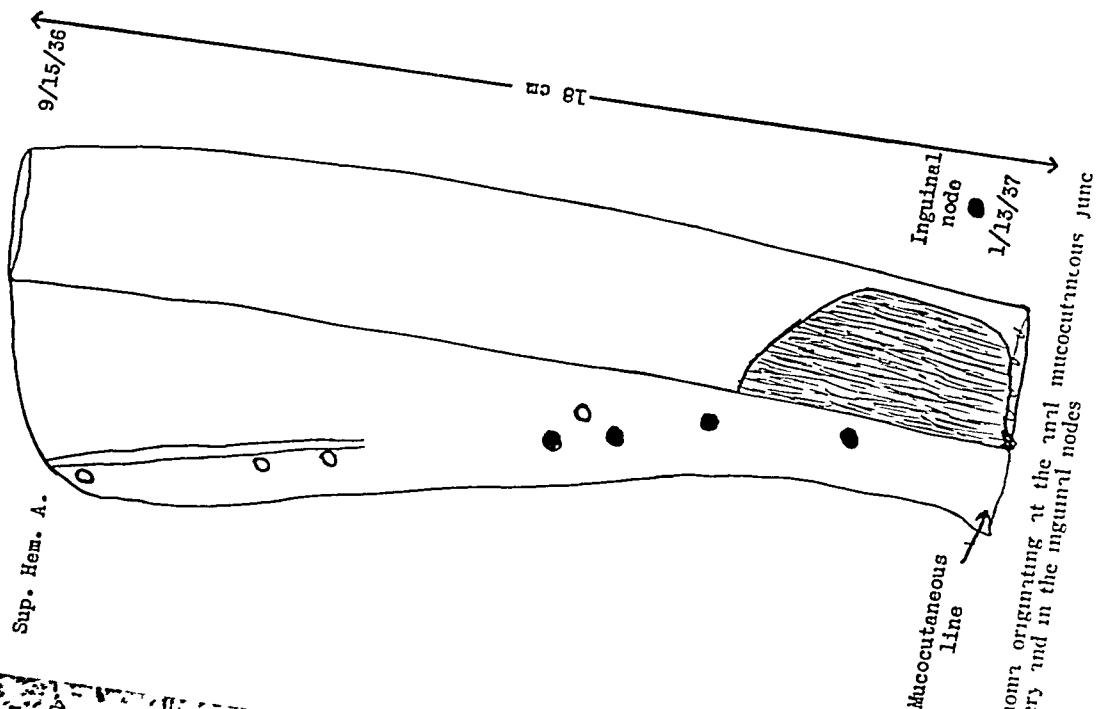


FIG 6—Hosp No 34446 Showing a double lymphatic drainage from a tumor situated at the level of the levator ani muscle, one node of the superior lymphatic drainage path and two nodes situated 2.5 cm laterally to the musculovis of the bowel being found involved



Fig 7—Hosp No 31289

Showing a double lymphatic involvement, metastases having occurred in both the lymphatic nodes accompanying the superior hemorrhoidal artery and in the inguinal nodes



(4) Where the tumor is found at the level of the levator ani muscle, there is a double lymphatic drainage the more common is upward along the superior hemorrhoidal artery, the other direction is laterally along the superior surface of the levator ani muscle. Lymph node metastases are found here. Four such instances occurred in this series. One has been cited above (Fig 5—Hosp No 33779). The specimen illustrated in Figure 6 is from a patient, age 53, who, while in the hospital recovering from fractures of both

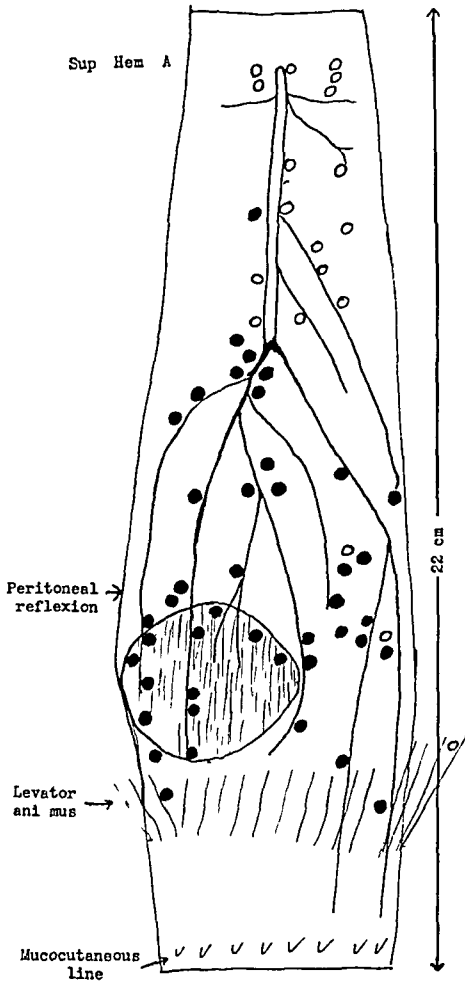


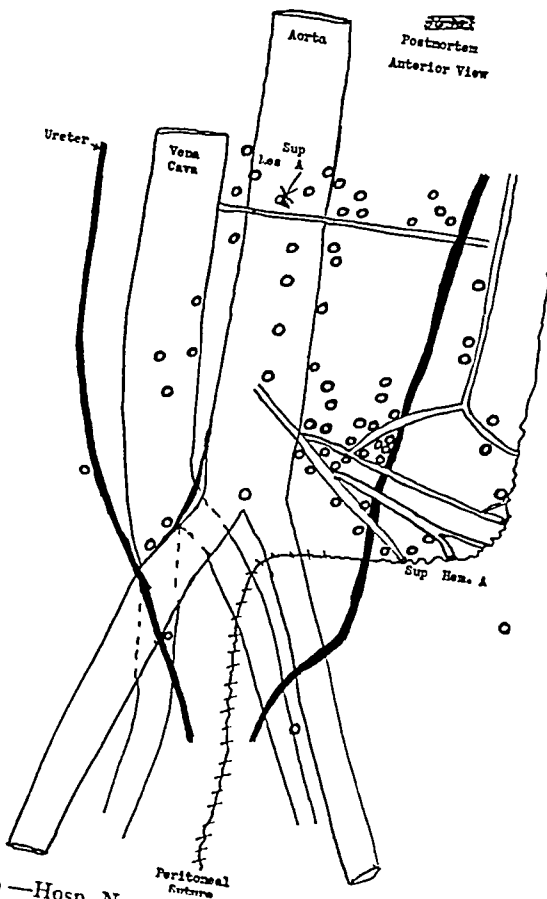
FIG 8—Hosp No 36303. Showing the extent, both superiorly and inferiorly that metastases can occur, and how essential a Miles type of combined abdominoperineal resection is, if one wishes to eradicate them.

the superior hemorrhoidal artery as high as possible and wide resection of the levator ani muscles, is necessary in order to give the best chance of permanent cure. Figure 8 illustrates the specimen removed from a patient, age 64, who had had symptoms for 12 months. The tumor was ulcerating, and involved 60 per cent of the circumference of the bowel. It had penetrated all coats of the bowel and was slightly adherent to the fascia propria. Nodes were palpable in the hollow of the sacrum. A Miles type of combined abdominoperineal resection of the rectum was performed. Sixty-two nodes were

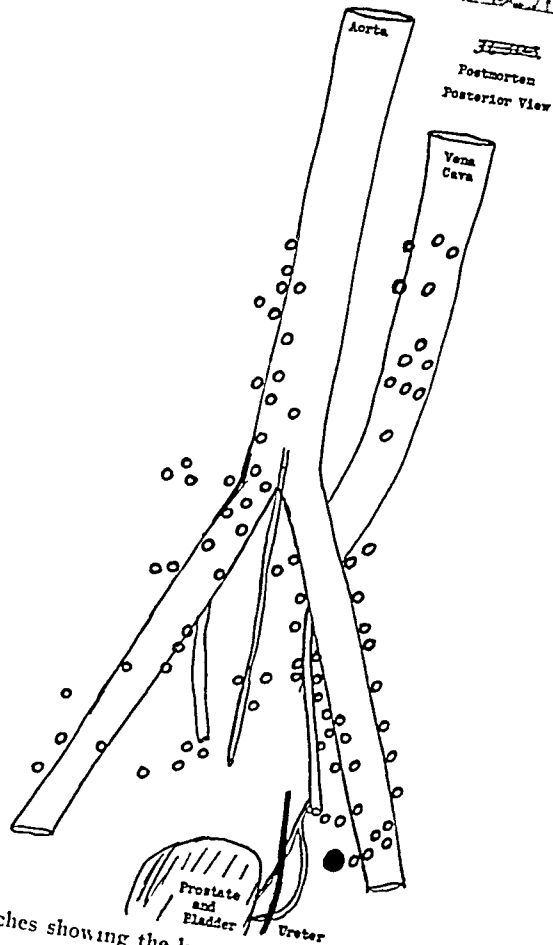
legs, developed rectal bleeding. Six weeks later he was operated upon for carcinoma of the rectum. The tumor involved 50 per cent of the circumference of the bowel. Eighteen nodes were found by gross dissection, three of them being involved by carcinoma. The two along the levator ani muscle were 2.5 cm lateral to the muscularis of the bowel.

(5) Squamous cell carcinomata which involve the mucosa may have a double lymphatic involvement. Figure 7 illustrates the specimen removed from a patient, age 60, who had had symptoms for six weeks. The tumor originated at the mucocutaneous line and extended upward for 5 cm involving the mucosa but without producing any ulceration. There had never been any bleeding. It involved about 80 per cent of the circumference of the bowel. Eight nodes were found by gross dissection, four of them along the course of the superior hemorrhoidal artery, above the tumor, were involved. Four months later the inguinal nodes were removed and one of them showed metastatic involvement.

(6) Postmortem examination shows that radical removal, with resection of



Postmortem
Anterior View



Postmortem
Posterior View

FIG 9—Hosp No 36303 Autopsy Anterior and posterior sketches showing the lymph node distribution

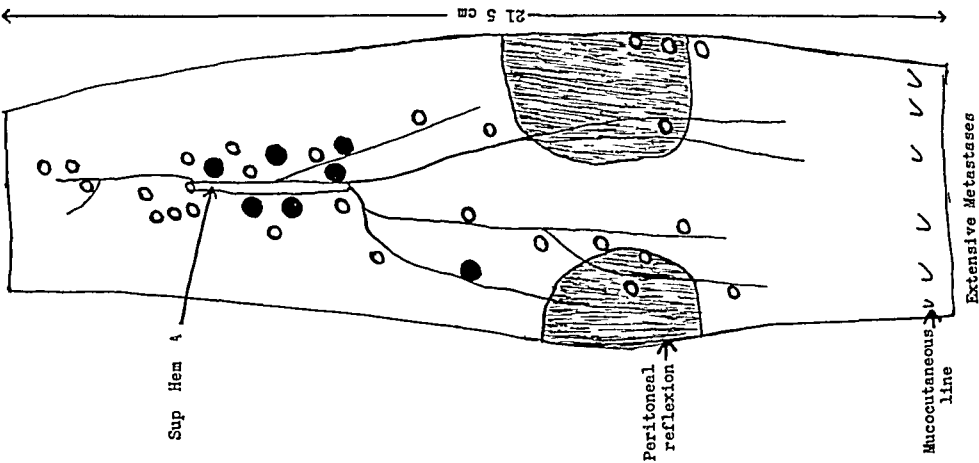


FIG 10.—Hosp No 36642 Showing the high distribution of the involved lymphatic nodes



CARCINOMA OF RECTUM

found, 43 of them showed metastases. The highest node involved was only 3 cm below the point of ligation of the superior hemorhoidal artery. He had an uneventful postoperative course until the eighth postoperative day,

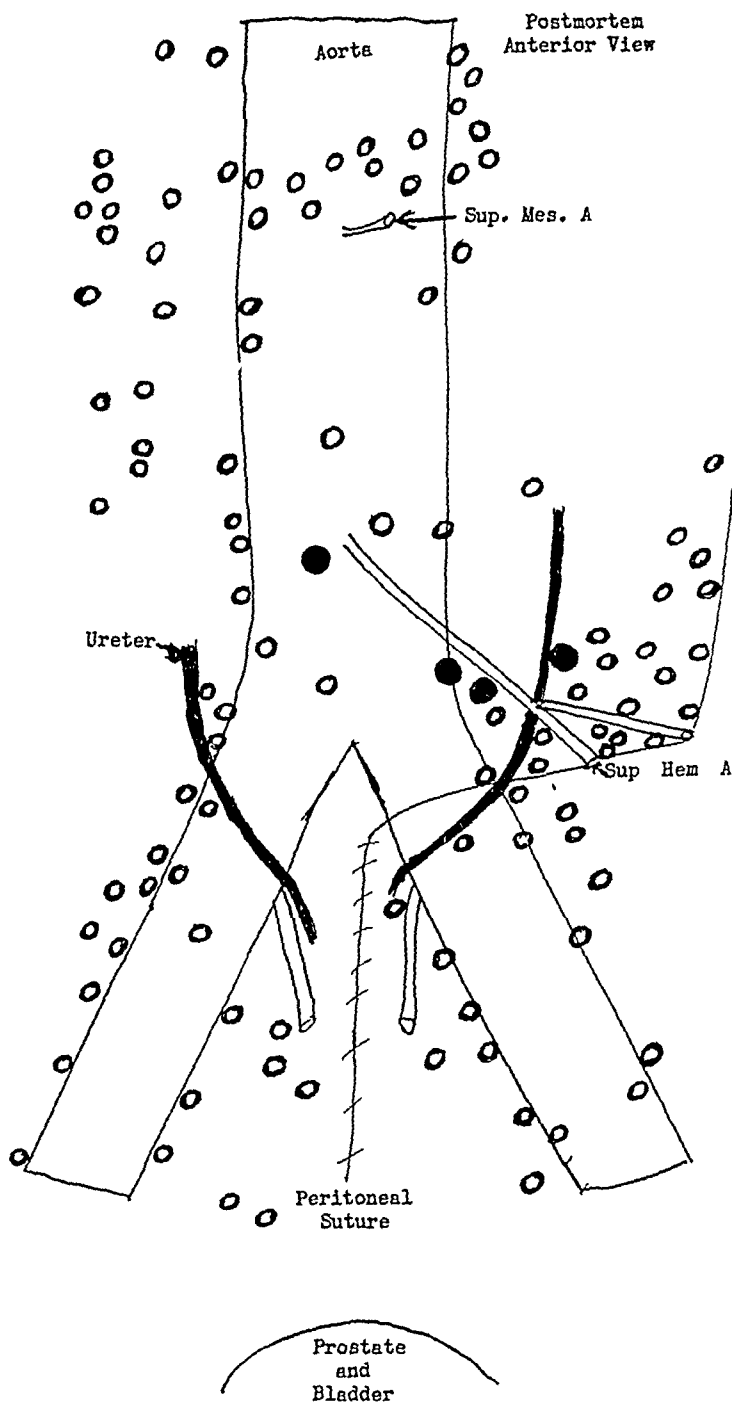


FIG 11—Hosp No 36642 Autopsy Sketch showing the lymphatic node distribution, and the presence of involved nodes remaining postoperatively, which would have been impossible of surgical removal

when he suffered a massive pulmonary embolus and died. The two diagrams of the postmortem preparation show the location of the 160 nodes which were examined. The highest node was 3 cm above the point of origin of the superior mesenteric artery, and the lowest was at the inferior border of the prostate, as far distal as it is possible to cut the arteries from within the abdo-

men In spite of the extensive lymphatic involvement in the operative specimen, there were no metastases above the point of resection. The one node involved was about 1 cm lateral to the widest point of resection, along the levator ani muscle (Fig 9).

Figure 10 illustrates the specimen removed from a very thin and feeble patient, age 72, who had had symptoms for six months. The tumor involved 65 per cent of the circumference of the bowel. There were a number of enlarged nodes high up, and because of a peculiar congenital peritoneal anomaly, the superior hemorrhoidal artery could not be resected as high as it frequently is. Thirty-five nodes were found in the operative specimen, seven of them contained metastases. He died of an aspiration bronchopneumonia. The diagram of the postmortem preparation shows the location of the 111 nodes which were studied. Four nodes were found to be involved, demonstrating that a complete removal was not possible in this case.

CONCLUSIONS

Prognosis based on the spread of the tumor into the lymph nodes is inaccurate unless a careful dissection of the specimen is made.

When a very careful search for lymph nodes is made, either by gross dissection or in the cleared specimen, about 68 per cent of all operatively removed specimens of carcinoma of the rectum will have metastases to lymph nodes, and the more nodes examined, the greater the number per specimen which will show carcinoma.

Recognition of involved nodes by palpation is difficult or impossible where the nodes are small, since only 48 of 111 lymph nodes containing carcinoma showed any gross change, even in cross-section of the node.

Tumors which are questionably operable because of the large size of the tumor and because of obesity in the patient may have no lymph node metastases.

Small tumors may have very extensive lymphatic node metastases.

Tumors having lymph node metastases tend to be of a higher classification, according to Broders' grading, than those without metastases.

A high ligation and division of the superior hemorrhoidal artery, and of the lymphatics accompanying it, is desirable whenever possible, since low-lying tumors may have high-lying metastases.

Where there is gross enlargement of the high-lying nodes, with lymph blockade, there may be retrograde metastasis below the tumor.

Where the tumor is near the level of the levator ani muscles, those muscles should be resected as widely as possible, since metastasis along them seems to be common.

Squamous cell carcinomata metastasize upward along the course of the superior hemorrhoidal artery, as well as laterally to the inguinal lymph nodes, when the mucosa is involved. Therefore, a radical resection of the rectum should be performed whenever a squamous cell carcinoma has involved the mucosa.

The Miles type of operation seems the ideal one from the standpoint of wide removal of the lymphatic node bearing area

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DISCUSSION —DR VERNON C DAVID (Chicago, Ill) This is rather discouraging information. It seems to me practically to indicate that the more radical procedure attempted, and particularly the higher ligation of the superior hemorrhoidal artery we do, the more likely we are to be above nodes which are involved, no matter what the position of the tumor in the bowel may be.

We now are ligating the superior hemorrhoidal artery just distal to the first sigmoid branch, which usually, in the average patient, is about two to two and one-third inches above the promontory of the sacrum.

One other fact that seems to me of practical importance is that where nodes are palpable (and this work shows that they are not all palpable that are involved), and presumably involved, there seems to occur a blockade of the normal spread of the disease along the vessels, and detours are made in which nodes may occur in the retrograde lymphatic group as well as the lateral group, and therefore it has seemed to us that in cases of that type, we should start our dissection laterally at the level or plane of the ureters and work toward the bowel.

I feel very sure that there are other lymphatics than those described so adequately by Miles that traverse the well known routes described by him. I am sure that all of us have seen carcinomata on the anterior wall of the bowel of women where, without much adherence to the rectovaginal septum nodules have been found in the vaginal mucosa.

About a month and a half ago, we saw a woman for the first time with an otherwise operable carcinoma, the size of a dollar, on the lateral side of the bowel, not attached at all to the rectovaginal septum, that had a half dozen metastases in the vaginal mucosa. No others could be found. Therefore, that indicates that there may be other routes that are certainly not favorable, but I think they occur.

DR HARVEY B STONE (Baltimore, Md) I think that both Doctors David and Gilchrist certainly deserve a great deal of respect and admiration for the very painstaking and laborious piece of research which they have carried out. Doctor Gilchrist, out of consideration for our patience, did not describe the very laborious, time-consuming technique required to clean these specimens, to draw charts of each one of them, to label each node found, and then to correlate the microscopic study of those individual nodes with their position on the anatomic charts. It is really an overwhelming piece of work and certainly throws valuable and important light on a very practical and alive surgical problem.

Many of the observations which they recorded, of course, have been foreshadowed by the work of Miles and others, but it seems to me that there are certain new points or points of renewed emphasis that are well worth repeating in this brief commentary.

In the first place, I think that we have all realized that there was no close

correlation between the size of the primary growths and the metastatic involvement, but my own reaching of that conclusion had not been based upon the finding of involved lymphatic nodes but rather upon the fact that I think all of us must occasionally have observed that sometimes a quite small primary growth in the rectum is accompanied by palpable nodules in the liver.

I had always explained that to myself as an accidental invasion of the blood vascular system with direct embolic transportation to the liver, but now the work just presented shows that in addition to these presumably accidental metastases, one must routinely expect the possibility at least of widespread lymphatic extension from comparatively small primary growths.

Another thing that amazed me was the number of nodes found in these specimens. I had, from my own dissection and observations of specimens removed, concluded that an average of perhaps 15 or 18 nodes was the normal equipment of lymphatic apparatus in such specimens, and it is rather surprising to learn that, in this bulk of material, an average of more than 52 nodes was found per specimen.

Furthermore, I think that the important conclusion derivable from this entire work is the light that it throws on the still persisting controversy between the Miles type operation and that of Lockhart-Mummery or some sleeve-type of resection, in which either an attack from below or an effort to preserve the sphincter muscle is the purpose of the operation.

I do not believe it is possible, in the face of the evidence here presented, to feel that one has done everything possible to perform a radical removal of carcinoma of the rectum unless the Miles type operation is adopted as a standard procedure. It seems to me that with this evidence, no one can feel that a perineal resection by the Lockhart-Mummery or any other type of attack from below can give any assurance whatever that the metastatic nodular involvement has been removed.

I think another important observation made is this, that we have all been taught, and properly so, that because nodes were palpable, they were not necessarily involved. Now, there is an even more important corollary in these observations, which is that because nodes are not palpable, is no proof that they are not involved.

DR RALPH COLP (New York, N. Y.) I hesitate to show our series, because I think as you glance at the slides you will come to the conclusion that we probably have not been radical enough in our abdominoperineal resections, because the number of nodes which we found were far less, and certainly the number of cases which presented metastasis were fewer.

We originally started to dissect these nodes by the method advocated by McVay, Wood and Wilkie, but soon found we were missing a certain number, so we decided we would employ the method advocated by Westhue, which evidently is not as good as the one which Doctor David presented. The Westhue method is based upon a fixation in Kaiseiling I solution, then dehydration in alcohol, and then finally cleared in methyl salicylate solution.

Up to date, Dr. S. H. Klein in our laboratory, under Doctor Klemperer's direction, has examined 18 cases, which I would like to present.

Table I details the findings in these 18 cases, all but two of which were operated upon in two stages by the Lahey procedure. We found some cases with only nine, 14, and 17 nodes and others with 30, 34 and 45. It is rather interesting that the case in which the fewest nodes were present was one in which a perineal resection was performed because we felt that the patient would not tolerate an abdominoperineal resection, and it is quite obvious that a great number of nodes were left behind. In another case in which only nine

CARCINOMA OF RECTUM

TABLE I

CARCINOMA OF THE RECTUM AND RECTOSIGMOID*

Case No	Lymph Nodes Found	Lymph Nodes Containing Metastatic Carcinoma
55620	34	5
11239	9	0
57590	11	0
57702	45	0
55869	30	0
59575	17	4
55802	14	0
51747	19	7
8260	4 (Hartmann operation)	0
58428	14	0
53763	15	0
57763	1 (Jones perineal resection)	0
59044	13	0
53809	28	0
57618	3	0
11679	22	0
51915	9	0
56108	16	0

* The two stage Lahey procedure was performed in all cases unless otherwise specified

nodes were found, a Hartmann type of operation was performed, in which the lower rectal segment was left in place

Another interesting point in this series is the paucity of metastases. In one case in which 34 nodes were found, only five were involved. In other cases, there were 17 with four, 19 with seven, and 22 and 28 nodes without metastases. In spite of the fact that all of these nodes were very carefully examined, no metastases were found.

I agree with Doctor David that very often a retrograde metastasis may be present due to the plugging of the lymphatics, and in this series, two such cases were found. Westhue, in his report, stated that in 74 cases he found only one instance in which there were retrograde metastases and felt this could be discarded as having no clinical significance. However, in this series in which only three cases showed metastases, two of them showed evidence of retrograde metastases.

Figure 1 illustrates the nodes found in one case. One will notice that some of these nodes were found distal to the tumor, and one node was at a distance of 5 cm. In the second case which we had, one of these nodes was found at a distance of 3 cm.

I think if these retrograde metastases can happen in a small series of cases, such as we have reported here, it certainly emphasizes, again, that the only

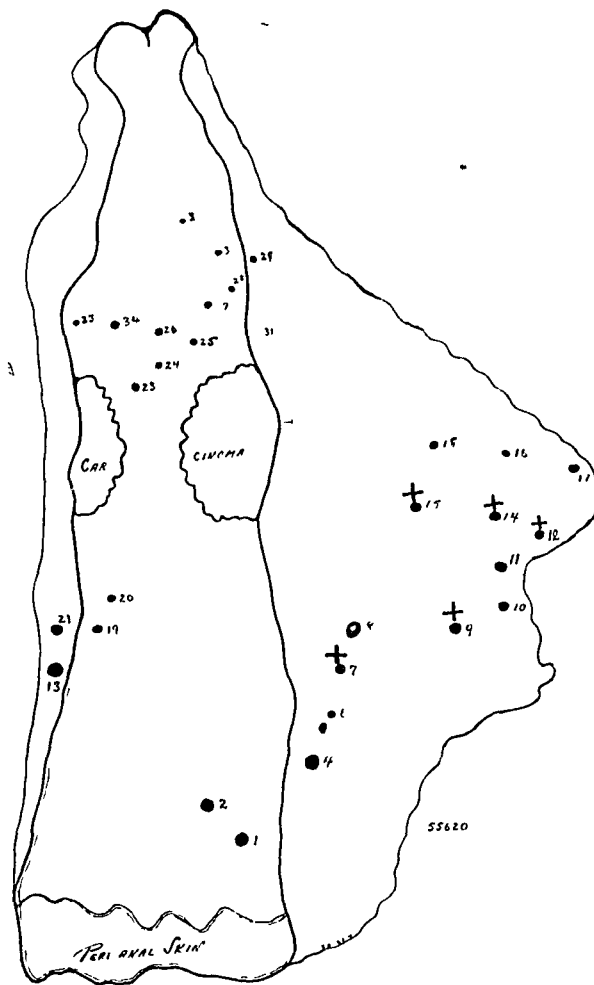


FIG 1—Schematic drawing of resected rectum and rectosigmoid. The numbered dots represent the regional lymph nodes. The nodes marked with plus signs exhibited metastatic carcinomatous involvement. Note that the positive nodes are situated distal to the primary growth.

type of operation which should be performed is a radical abdominoperineal resection, extending rather than some conservative types of procedure, in which an attempt is made to preserve the sphincters.

DR EDWARD ARCHIBALD (Montreal, Canada). This paper of Doctors David and Gilchrist forms a welcome addition to our knowledge of the spread in the lymph nodes in cases of rectal cancer, and one naturally asks oneself whether their findings modify in any way the view generally held in this country that Miles' abdominoperineal operation is superior, in ultimate results, to the Lockhart-Mummery resection of the rectum from the perineal side. In the paper under discussion I noticed one thing particularly that, although the lymph nodes adjacent to the cancer might be found free of disease, a node situated farther up might be involved. Such a fact tends to support the more extensive removal of the Miles operation. There remains, of course, the consideration of the question of operative mortality, and I think we must count it true that the Lockhart-Mummery will always show a better mortality rate after operation than the Miles procedure.

One other point in the present paper draws my attention—the relative infrequency of a spread of the lymph node extension downwards, that is, toward the anus, and this brings up once more, at any rate in the case of cancer situated three inches or more above the anal passage, the question of saving the sphincter. In 1907¹ I devised an operation which I hoped would combine the advantages of a complete block dissection of rectal cancer through the abdomen, with the preservation of the sphincter. It involved the mobilization of the descending colon and at times even of the splenic flexure and the section of the sigmoid mesentery far back, at the peritoneal reflection, so as to preserve the vascular supply in the arcades. The mobilized sigmoid was brought down and sutured to the anal stump of the rectum. I finally gave up the operation because it was difficult to be sure of the maintenance of arterial circulation in the sigmoid mesentery under the operative conditions of those days, when we did not know how to prevent operative shock, and patients such as these often came off the table with a very low blood pressure, lasting for hours and a consequent imperfect circulation in the sigmoid stump. Injection experiments in the cadaver, it is true, had demonstrated the patency of the vessels in the sigmoid segment, when brought down without tension to the anal stump, but the injection experiments had not been made at low pressures, had indeed been made probably under a pressure far higher than even normal blood pressure, that is, with a syringe. The result, clinically, was too often necrosis of the sigmoid stump, failure of union, and ultimate obstruction from scar. During the past few years I have often thought that one might perhaps under improved operative conditions as regards blood pressure return to this operation and again make the attempt to save the sphincter. But two considerations still tend to block that path, at any rate still offer obstructions that must be surmounted. Of these, the first is the difficulty of securing primary healing of the anastomosis between the sigmoid and anal stumps, not only because of the possible risk of imperfect circulation but also because of the risk of infection. Our modern methods of aseptic bowel suture after resection are hardly feasible in the depths of the pelvis, whether one tries it from the abdomen or from the sacral side. And secondly, modern apparatus has succeeded in making the abdominal permanent colostomy very much less of a trial to the patient than in earlier days. There are still patients, and not a few, who say before operation that they would rather die than have a permanent colostomy. On the other hand, there does exist the diametrically opposite view, and, if you will allow me to conclude on a somewhat lighter note, I would quote the remark of a patient, recorded by one of our Paris colleagues years ago, concerning the annoyance of the artificial anus and the philosophic resignation which that was supposed to demand. This patient, finding that her colostomy was working decidedly well, and that she was not annoyed to anything like the degree which she had expected, said to her surgeon as he paid the final visit: "Doctor, I don't see why the good Lord didn't put our behinds in front, it's much more convenient!" If all of our patients were able to adopt the mental attitude illustrated in this French lady's observation, the chief opposition to the radical operation, with its permanent colostomy, would be overcome. Nevertheless, it is certain that many perfectly reasonable people will continue to view an artificial anus as one of the great trials of the flesh. In this sense I still think that there will occur a swing back to some method of preserving the sphincter, when the cancer is

situated not too near to the anal passage. Such methods, of course, have been devised and published, but at present they seem to be relegated to the lumber-loft, in favor of the abdominoperineal and perineal methods.

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ARTERIOVENOUS ANEURYSMS

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IN 1925, Reid¹ published a series of four papers under the general title of "Studies on Abnormal Arteriovenous Communications, Acquired and Congenital." In these articles the literature of the subject was rather extensively reviewed. He put forward the thesis that there was no essential difference, except in the size and number of arteriovenous fistulae, between angiomata cirsoid aneurysms and arteriovenous aneurysms, and this view has been rather generally confirmed.

Thirty-three cases were reported and the clinical studies of them, together with laboratory investigation formed the basis for certain remarks concerning the effects upon the body of abnormal arteriovenous communications, and their treatment. At that time the author realized that there were many matters in connection with this subject which had not been solved, that further investigations of it would yield important physiologic, pathologic and therapeutic observations. This has not only proven to be true, as witnessed by the important contributions upon the subject, but has led to by-paths which give promise of yielding important observations concerning conditions which are more frequently encountered than are abnormal arteriovenous communications. We have in mind cardiac disabilities especially aortic insufficiency and cardiac failure, the state of the capillary bed, the normal absence of capillaries in certain parts of the human body and of other animals,² blood volume, circulation time, *etc.* Indeed, rarely has the investigation of such an infrequent clinical condition been so fruitful of important collateral contributions. This field of investigation seems limitless, for new problems always present themselves, and there are still many old ones which have not been solved.

The purpose of this report is to present another series of 30 cases (12 in detail), to discuss our clinical observations and surgical procedures and to supplement, whenever pertinent, these clinical studies from observations made in our laboratory of experimental surgery.

In this paper are included all the cases we have had since Reid¹ published his series of 33 cases, in 1925. Several of this series have been published previously in considerable detail and are included here only in the synopsis of cases (Table I). Where this has been done full reference is given to publications in which complete details may be found. They are included here again for two reasons. First, we wished to use data from them in our general discussion of the subject of abnormal arteriovenous communications, second, later observations on these cases may be of interest to someone. None of the 12 cases reported in detail in this paper has ever been published before.

Case 13—Massachusetts General Hospital No 29001 and No 29001 R A This patient was first admitted to the hospital May 5, 1931 At that time he was 31 years old At about the age of 15 he injured his right leg with a hand sickle The point of the blade entered the anterior surface of the leg lateral to the tibial crest and about two inches below the tibial tubercle There was profuse bleeding which was controlled by a tourniquet until the wound was sutured During the following years there was no disability, but the patient noticed that the right leg was a little larger and possibly longer than the left There was no shortness of breath, even when rowing at college or when skiing

The patient first came for examination because of the accidental discovery of a tumor, thrill and bruit in the region of the old sickle scar, when he was examined and treated for a sprained ankle Shortly after this he came to Dr A W Allen of Boston for the treatment of an arteriovenous aneurysm On his first admission to the hospital moderate varicose veins were noted, the right calf measured 38 cm and the left 35½ cm, heart sounds were normal, blood pressure 140/80 Maximum pulsation, thrill and bruit were noted in the popliteal space, but the bruit could be heard over the entire femoral artery and its branches, as well as all about the knee and just below it

Operation—May 8, 1931 Doctor Allen ligated and divided a large artery, low in the popliteal space, which he thought to be the posterior tibial The vein was not disturbed and great care was taken not to injure the posterior tibial nerve The actual fistula was thought to be lower in the leg, but inasmuch as the ligation of the artery caused the thrill and bruit to disappear, no attempt was made to close it After the completion of the operation, a pulse could be felt in the anterior tibial artery

Two weeks after this operation a "toe-drop" developed and an area of anesthesia on the dorsum of the foot and ankle could be demonstrated Some reddened areas just above the ankle were noted and they soon developed into a chronic ulcer which would not heal and occasionally bled profusely A soft bruit and later a thrill made their reappearance in the region of the old stab wound

During the year following this first operation the signs of an arteriovenous aneurysm became progressively more pronounced until they were almost as evident as before the operation The patient wore a brace with a right-angle ankle stop for his partial peroneal nerve palsy, the ulcer refused to heal and occasionally bled During this year it was necessary for him to use crutches all of the time In October of 1931, Dr F R Ober noted a barely palpable pulse in the dorsalis pedis artery and a good pulse in the posterior tibial In addition to confirming the diagnosis of partial paralysis of the peroneal nerve, he observed that a shortened Achilles tendon limited dorsal flexion of the ankle about 20 degrees

About a year after the first operation Doctors Allen and Reid saw this patient together The circulation of the foot and ankle was definitely impaired, although feeble pedal pulses could be felt The chronic ulcer above the ankle was about the size of a silver dollar, grayish, cyanotic in appearance and exhibited no evidences of healing In the skin about the knee and upper leg the veins were so numerous and distended as to give an angiomatic appearance Anteriorly at the site of the stab a forceful pulsation could be felt Here and all about the knee was a distinct thrill The loud continuous bruit, with systolic intensification, could be heard, with diminishing intensity, up to the groin and down to the ankle The femoral and popliteal arteries appeared to be two or three times their normal size Occlusion of the arteriovenous fistula by direct pressure caused, after a very short time, a definite increase in the volume of the pedal pulses and a slowing of eight to ten beats in the heart rate The action of the heart was regular and no enlargement was demonstrated by physical examination At the time of these studies (May, 1932) an extirpation of the fistula was advised

Second Operation—August 9, 1932 Doctors Allen and Reid The duration of the operation (five hours) bespeaks the tediousness of the procedure and the great vascularity brought about by the secondary angiomatic condition of the tissues, as well as the

technical difficulty of attacking directly an arteriovenous fistula situated at the bifurcation of the popliteal artery. Figures 1 and 2 make unnecessary an extended description of the operative procedure. The approach, as in the first operation, was again made

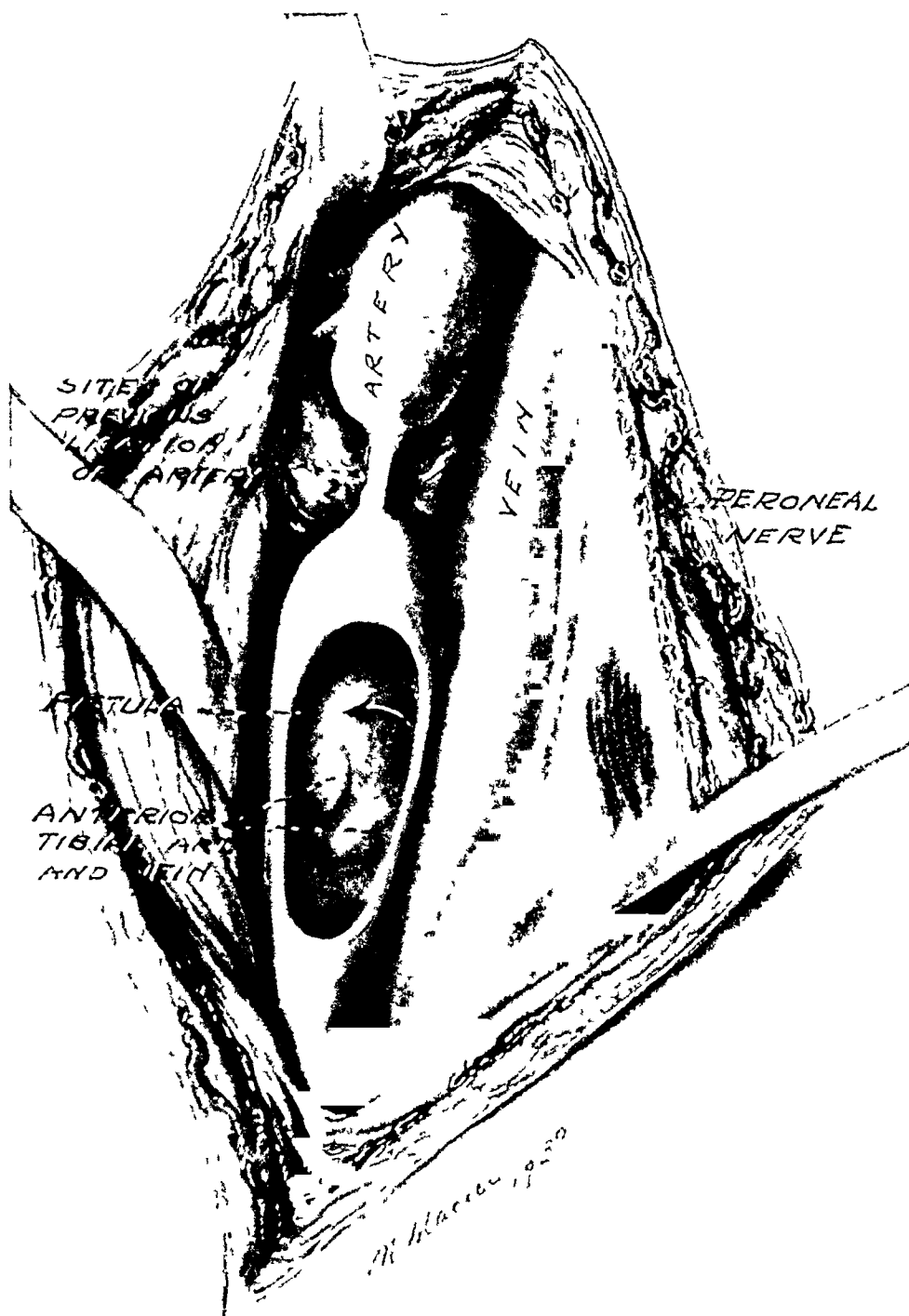


FIG. 1.—Case 13. Arteriovenous aneurysm between popliteal vessels at the level of origin of the anterior tibial vessels. The artery was ligated 15 months before this operation. The peroneal nerve is infiltrated with large blood vessels which caused its partial paralysis.

through the popliteal space. The popliteal artery was about three times its normal size and very thin-walled, it was completely occluded about one inch above its bifurcation. The enormous popliteal vein was intact and through its wall could be seen the play of mixing arterial and venous blood. The peroneal nerve presented a remarkable an-

giomatous appearance, as if threads of veins had been woven throughout the five or six inches which were exposed. In the absence of neuromata or any evidence of scarring

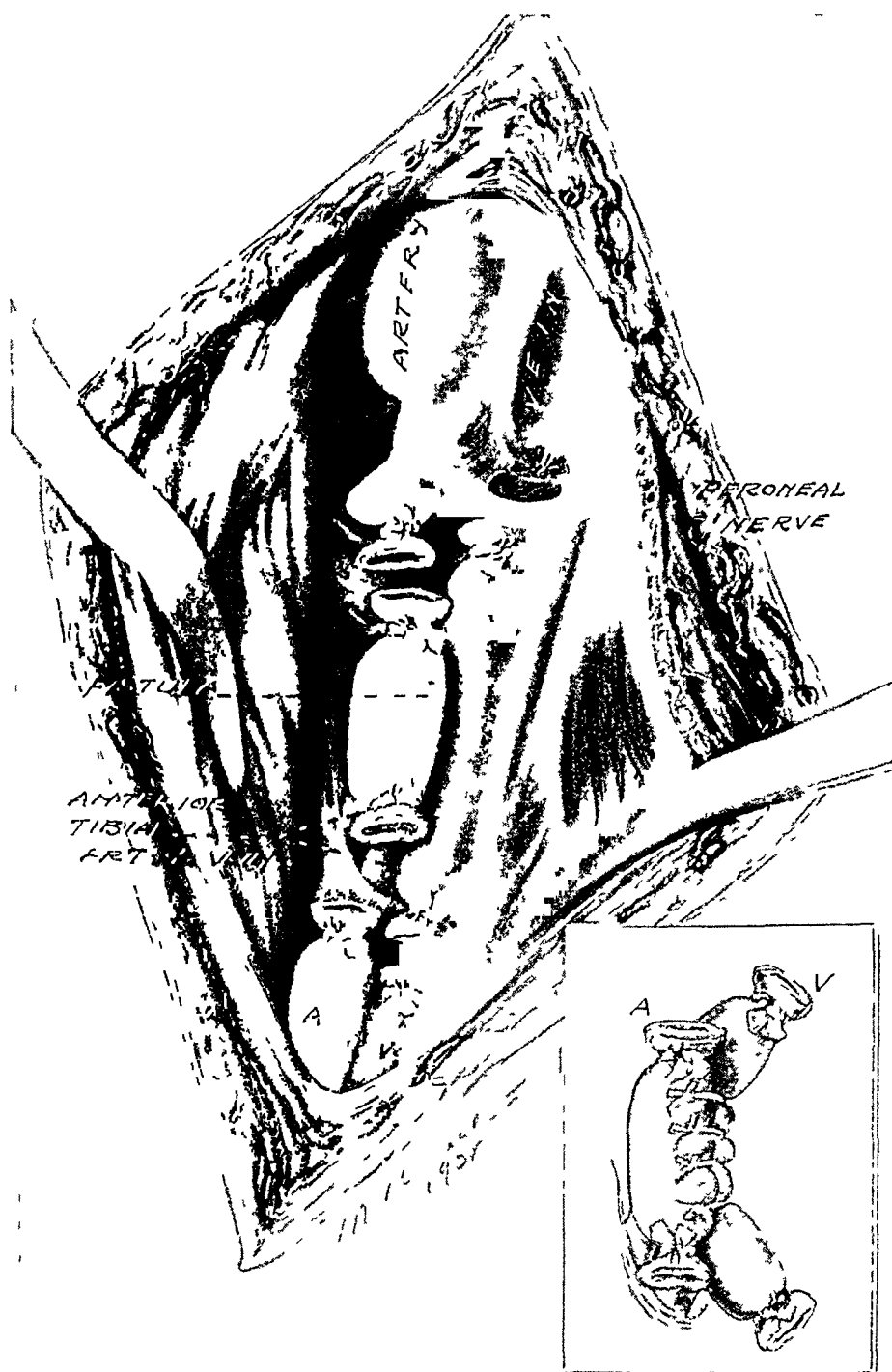


FIG 2—Case 13. The operation as completed. The quadruple ligations were effected with tape and anchored with transfixion sutures of silk. The fistula was closed with transfixion sutures (see insert) of braided silk because of the technical difficulty of exposing the anterior tibial vessels from a posterior approach.

or injury, we attributed its partial paralysis to this vascular change within it and, as we shall see from future observations, that was correct. The fistula was just at the bifurcation of the popliteal artery and vein—a very difficult situation because of the

fixation of all vessels at this point by the opening in the interosseous membrane. It was not particularly difficult to free the popliteal vessels down to the point of their bifurcation and the site of the arteriovenous aneurysm, with more difficulty the posterior tibial vessels beyond the communication were dissected free. The fistula being located practically in the foramen of the interosseous membrane, the freeing of the anterior tibial vessels from a posterior approach presented a vastly more difficult problem and would have resulted in prolonging the operation considerably. Finally it occurred to us to terminate the operation as illustrated—ligation and division of the popliteal vessels near the fistula, ligation of the posterior tibial vessels just beyond the fistula, and transfixing occluding sutures of the fistula just opposite the origin of the anterior tibial vessels. The fistula was not excised. At the conclusion of the operation no thrill could be felt, with a sterile stethoscope no bruit could be heard. Throughout the operation silk and tape, varying in size to correspond to the size of the vessels to be ligated, were employed. The wound was closed with fine silk, without drainage.

At the completion of the operation the circulation of the foot appeared better, the pedal pulses stronger, and the granulations of the ulcer redder and more healthy. The operative wound healed without any complications. Five days after the aneurysmal operation the patient developed acute appendicitis and was operated upon for it. Except for this his convalescence was exceedingly easy and he was discharged 17 days after admission.

Subsequent Course—The circulation in his foot continued to improve and the ulcer promptly began to heal. Three months after the operation, it was completely healed. On November 22, 1932, Doctor Ober performed a "Z" plastic operation to lengthen the Achilles tendon. Within six months all evidence of any paralysis of the peroneal nerve had disappeared. At the present time (November 1937) the patient has no disability or evidences of circulatory embarrassment in the right leg. There are no signs of an arteriovenous fistula.

In the interval between the first and second operations, the patient was confined to the use of crutches in order to get about, within a year after the second operation, he was again skiing and enjoying his usual sports without any apparent disability.

Case 24—Cincinnati General Hospital No 73329. A colored man, age 30, was admitted to the hospital April 16, 1937, with an enormously enlarged heart, auricular fibrillation and cardiac decompensation. He was dyspneic, the liver was enlarged and there was ascites. Rales were present at the bases of both lungs. A loud systolic murmur could be heard over the heart. The left leg was swollen and edematous. A large arteriovenous aneurysm was evident in the left groin at about the level of the profunda femoris artery (Fig 6). The artery proximal to this point was enormously dilated. Pulse was very irregular, averaging about 79 at the wrist, but there was a marked pulse deficit. Blood pressure 160/50.

Fifteen years previously he had received a gunshot wound in the left groin, which was not followed by severe bleeding and did not require hospitalization. The patient performed hard manual work as a railroad fireman until four months before entering the hospital, although on careful questioning he had had some dyspnea for the previous two years. The patient dated his illness back only four months when he was forced to go to bed because of dyspnea, anginal attacks, and swelling of the abdomen. After a short rest he resumed work but was soon forced to bed by another attack of cardiac decompensation and severe cardiac pain. This story repeated itself once or twice until, finally, after being in bed for ten days he agreed to come to the hospital.

Two days after admission to the hospital he had a chill, his temperature rose to 101° F, the left leg became markedly swollen. He evidently had developed extensive thrombophlebitis in the left leg. Another chill occurred three days later, the ascites increased, the patient became progressively worse in spite of all therapy which included, principally, morphine for his pain and digitalis for his cardiac failure. He became cyanotic and orthopneic, a severe cough developed.

On April 21, 1937, five days after admission, his venous pressure in the right arm was 25 cm of water with no change after occlusion of the aneurysm. Three days after entering the hospital his blood pressure, with the fistula open was 140/40, and with it closed 190/90. During this test it was noted that pulses became palpable in the foot when the fistula was occluded.

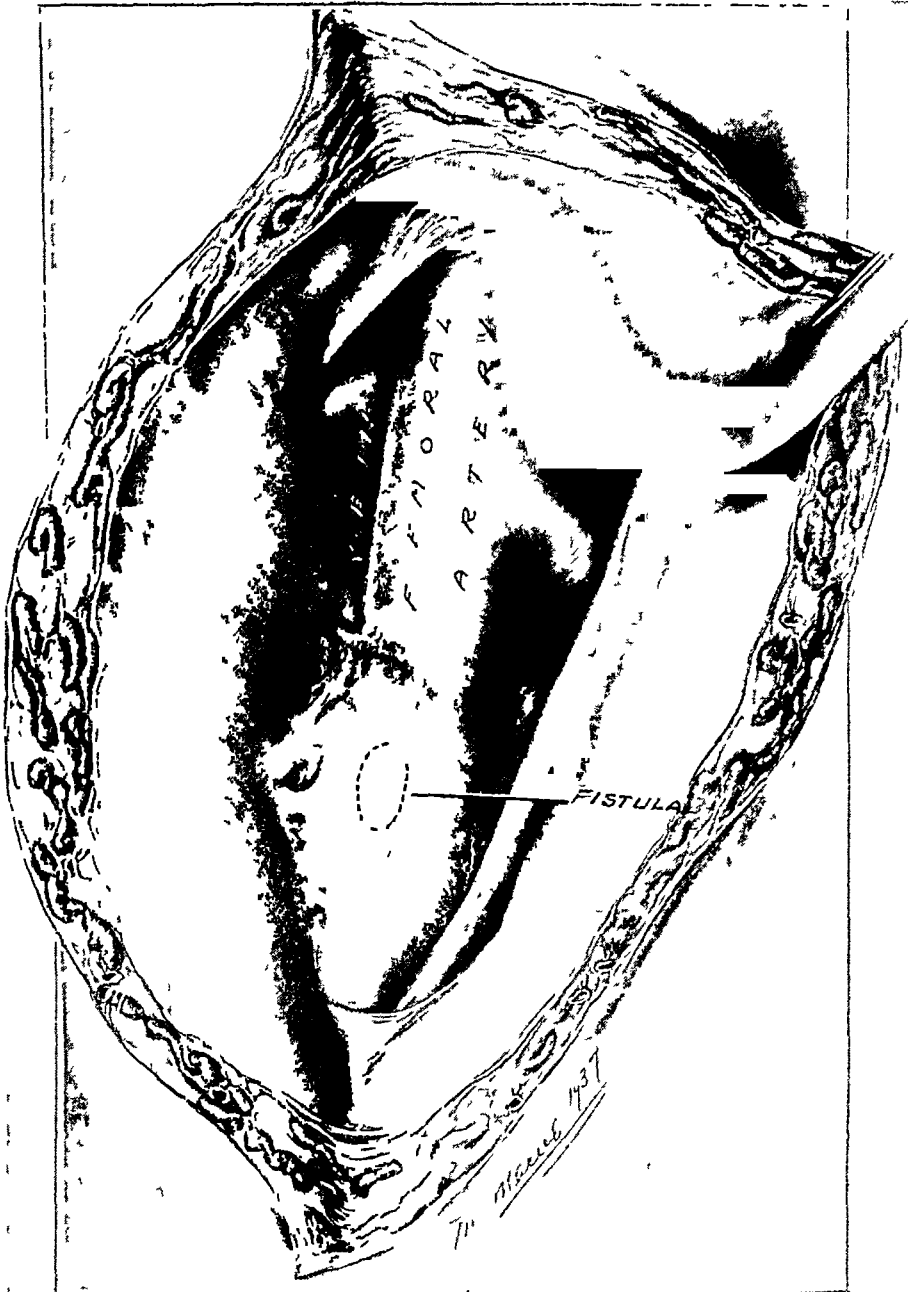


FIG 3—Case 24 Enormously dilated vessels exposed, revealing the region of fistula buried in dense scar tissue

With the patient steadily going down hill, and developing a decubitus ulcer, it was felt that his only hope was an attempt to eliminate surgically the arteriovenous fistula.

Operation—May 8, 1937 Under local anesthesia and with the patient in the sitting or orthopneic position, the operative procedure as illustrated in Figures 3, 4 and 5 was undertaken. The aneurysm was not excised, both because of the technical difficulties in

dealing with the vein and the serious condition of the patient, but the fistula was firmly occluded by transfixion sutures of braided silk, after dividing the artery proximal and distal to the fistula and ligating the vein distally (Fig 5)

The femoral artery was the largest artery Reid had ever ligated—more than one inch in diameter. Its wall was so thin that blood actually oozed through it proximally

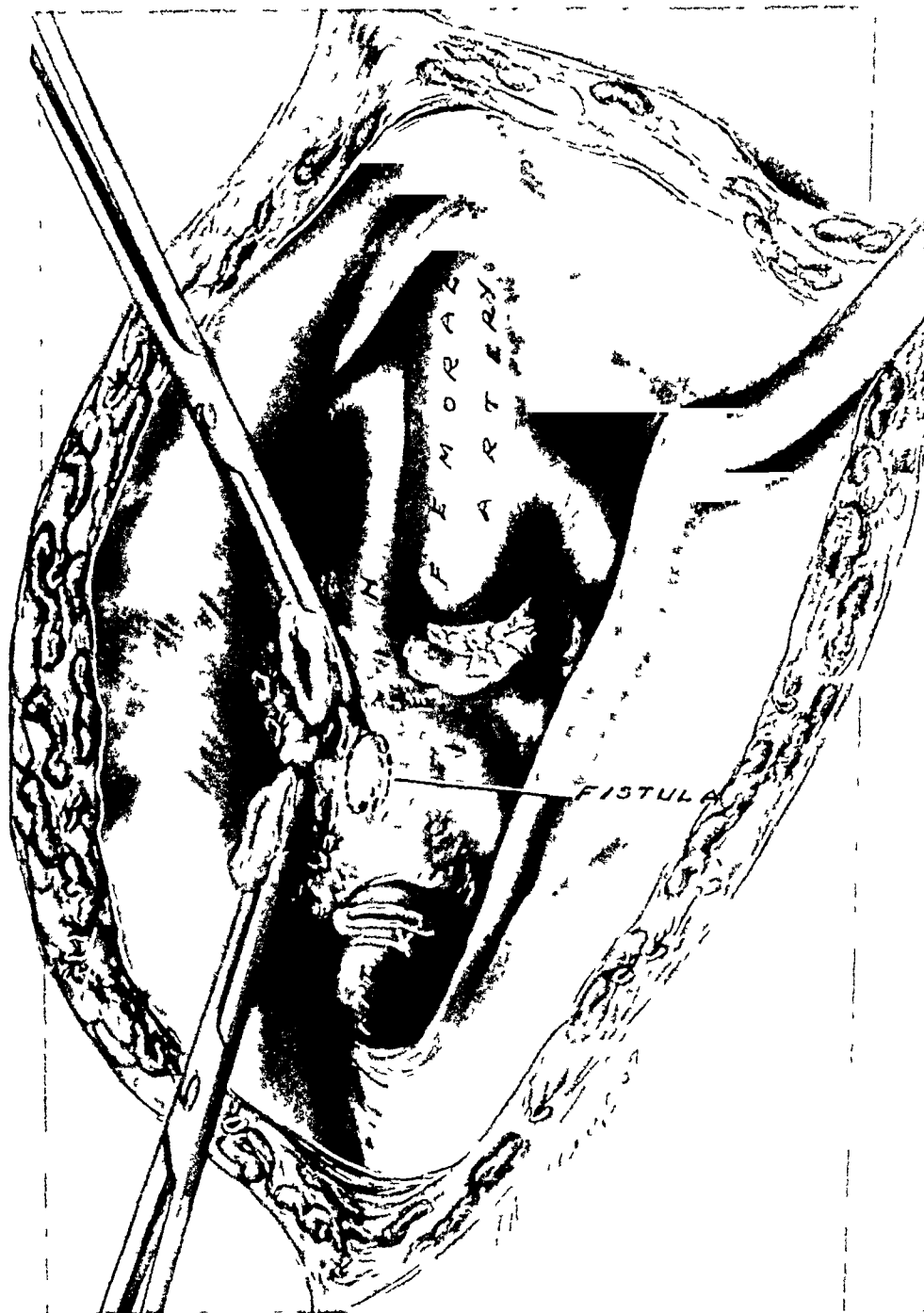


FIG 4—Case 24 Femoral artery above and below fistula divided, vein distal to fistula ligated

when the ligature of tape was tied. This was a precarious moment but fortunately the bleeding stopped under gentle pressure with gauze.

Immediately after eliminating the fistula the patient volunteered the information that his heart had not felt "so good in 15 years." The thin-walled, oozing artery was reinforced by an overlapping with Scarpa's fascia. The wound was closed with silk, with-

out drainage. The wound healed per primam, without any complications. The patient's postoperative course was uneventful, except for some fever for five days due to his phlebitis. The action of his heart became regular on the operating table and remained so afterwards. Three hours after the operation his pulse was 40 per minute. After remaining at this slow rate for two hours, it gradually began to rise to between 60 and 70 where it remained except for occasional lowering to a rate of 50. His blood pressure reached a peak of 190/100, two hours after the operation, and gradually came down to 130/90, where it seemed to be stabilized at the time of the patient's discharge from the hospital, 23 days postoperative.

Subsequent Course—This patient has been watched closely since leaving the hospital. The heart has decreased markedly in size, as shown by the teleoroentgenograms



FIG 5—Case 24. Femoral vein opposite fistula pierced with two strands of braided silk which were divided to form a V and then tied so as to occlude the fistula completely.

(Fig 7) The murmur has disappeared. The heart rate is regular at 80. Blood pressure 110/75. The venous pressure is 5 cm of water. The swelling of the leg has disappeared. There are good pulses in the left foot. The ascites has disappeared. The liver has returned beneath the costal margin. The patient is able to work without any difficulty except for the annoyance of an elastic stocking which he wears for varicose veins of his left leg.

Case 18—Holmes Hospital No 340642. A white woman, age 35, was accidentally shot April 17, 1934. The bullet entered the left scapular region, passed through the axilla and lodged in the left anterior chest wall. Immediately after she was shot, she was unable to move the left hand and arm, which felt numb. At the time of admission to her local hospital the hand had become swollen, and she developed a large hematoma, about the size of a "football," in the region of the left axilla. She was hospitalized for two weeks, during which time the arm was abducted and elevated. There was a gradual decrease in the swelling of the hand, as well as that in the axilla. The nerve sensation improved except for the areas innervated by the ulnar nerve, which apparently remained completely paralyzed. Before leaving the hospital she was conscious of a noise which she could hear in

her left ear. A loud bruit and thrill were demonstrable. She was told that she had an aneurysm.

She returned to the local hospital, May 18, 1934, and was operated upon, "at which time she lost a lot of blood." The bullet was said to be lodged in the vein at the site of the fistula. The vein was tied and the wound was packed with gauze. She remained in the hospital one month, and during this time there was considerable decrease in the swelling of



FIG 6—Case 24. Region of fistula before operation and ten days afterward. The curved incision was made in order to avoid the tremendously dilated veins.

the axilla and arm. About the middle of September, 1934, there was noted a return of the bruit and thrill. Also at this time there was a slight increase in the swelling of the arm, the veins about the shoulder became prominent. From that time on until her admission to the Holmes Hospital there was a gradual increase in the numbness of the left hand and, in addition to the paralysis of the ulnar nerve, she developed a typical wrist-drop, and practically a complete uselessness of the hand.

On admission to the Holmes Hospital, November 19, 1934, she presented a large swollen left arm, a big irregular scar which extended from just below the inner end of the clavicle to the humerus at the attachment of the pectoralis major muscle. About the

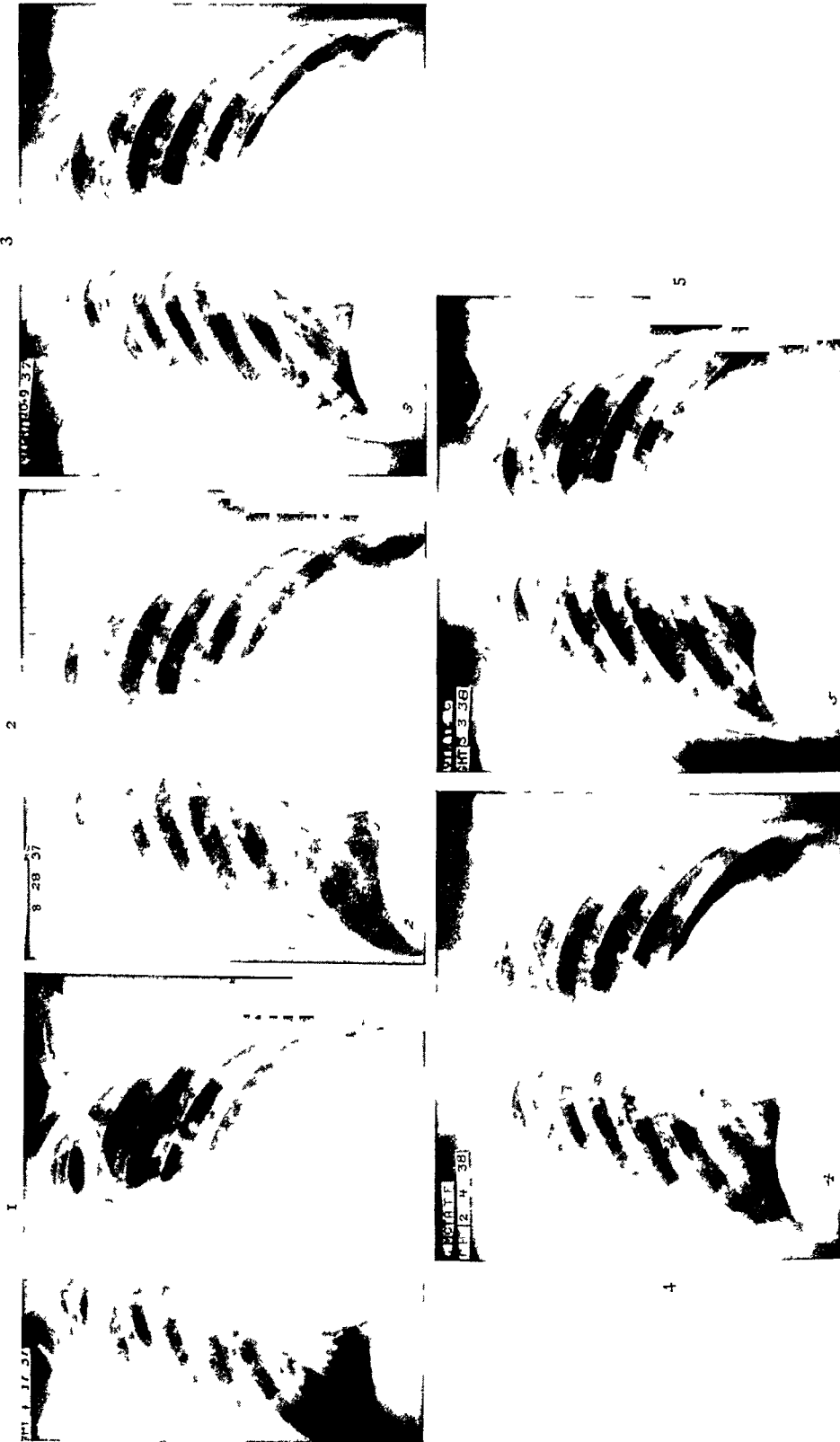


FIG 7—Case 24 Teleoroentgenograms of the heart No 1 Before operation No 2 Three and a half months after operation No 3 Five months after operation No 4 Ten months after operation No 5 Seven months after operation No 6 Ten months after operation No 7 Thirteen months after operation No 8 Seventeen months after operation

middle of this scar and approximately one inch below the clavicle, there was an area of pulsation accompanied by a very pronounced thrill and bruit. This bruit could be heard

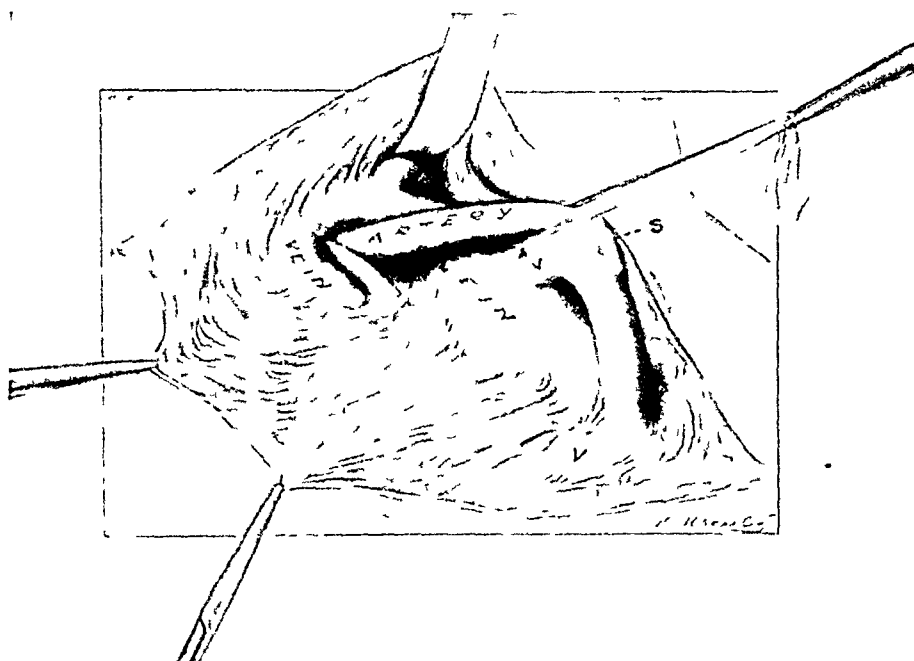


FIG. 8—Case 18. Artery held up showing the superior arteriovenous fistula, scar (S) in artery of previous inferior fistula, nerves buried in scar tissue, and blind ends of inferior vein comites.

down the arm to the left radial artery. There were no cardiac murmurs. The blood pressure in the right arm was noted to be elevated ten mm. of Hg. when the fistula was oc-



FIG. 9—Case 18. Artery resected and held up, nerves partially freed. Note scar in artery from previous operation and blind ends of inferior vein.

cluded by pressure. The pulse dropped from 86 to 72 on one observation, and from 100 to 84 on another when the subclavian artery was occluded. The fingers of the left hand

were markedly atrophied. The thumb was involuntarily abducted. The patient was unable to flex or extend the wrist. There was a moderate loss of sensation over the anterior aspect of the lower third of the left forearm. The blood pressure in the left arm

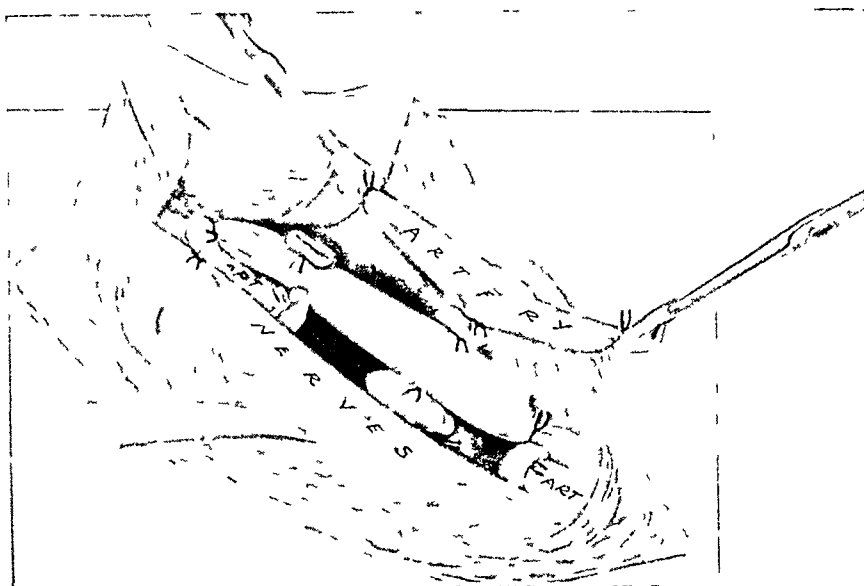


FIG 10—Case 18 Sites of ligatures in the process of excising artery and vein

was 88/56, in the right arm with the aneurysm open, 102/66, and with the aneurysm closed, 112/76. Oscillometric readings in the left arm were a maximum of 3 units and in the right a maximum of 5. The measurements of the left arm, after the swelling had subsided, showed a decrease of about 1 cm, as compared with the right.

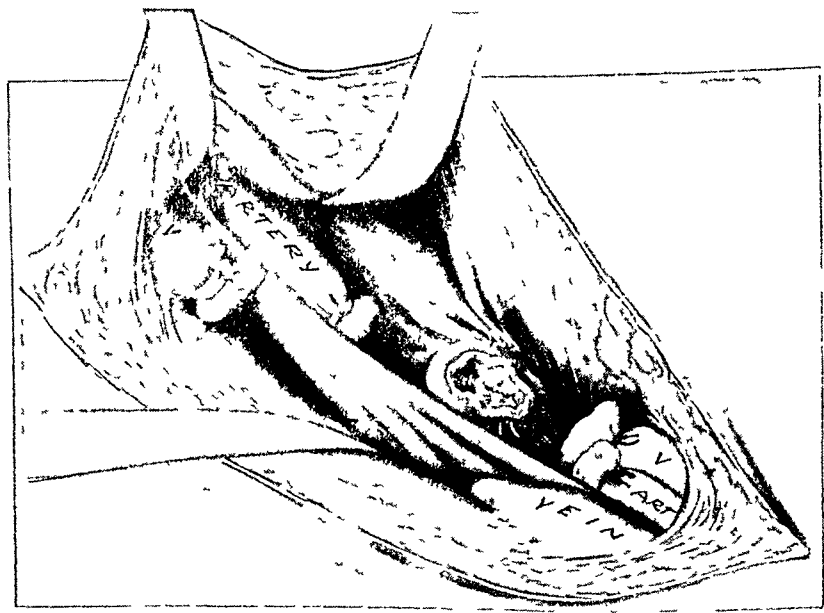


FIG 11—Case 18 Operation as completed. Axillary artery and vein excised, nerves freed

A teleoroentgenogram of the heart showed no definite enlargement, and there was no change in its size when the fistula was closed. On fluoroscopic examination there was no change in the size of the heart, even though a slowing of 20 beats per minute occurred when the fistula was closed.

Second Operation—Holmes Hospital, November 22, 1934. It required four hours

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of painstaking dissection to excise the scar tissue and to free the nerves, as well as to expose the site of the fistula. The operation is best appreciated by referring to Figures 8, 9, 10 and 11. A fistula was found between the axillary artery and a vein which lay above the artery. An old scar in the artery was also found, as well as the occluded vein, the result of the first operation. It was apparent that the bullet had pierced two veins and the artery, establishing a double arteriovenous fistula, that is, a communication between the artery and the vein above it and the vein below it. The first operation cured one of these fistulae, but had not affected the other.

After excising the scar tissue, which was exceedingly difficult to free from the nerves, the axillary artery and vein were removed. Silk was used for ligating the stumps of the vessels. The wound was closed without drainage. Following the operation there was no impairment of circulation to the hand, in fact, it was definitely improved, although

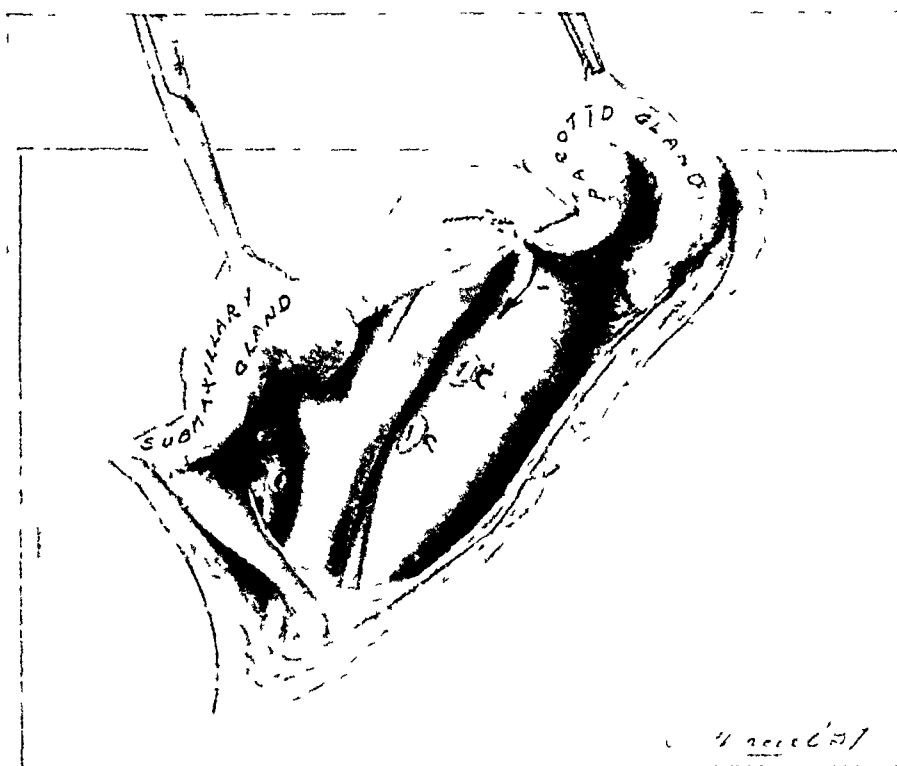


FIG. 12.—Case 23. Arteriovenous fistula at base of skull. Impossible to dissect jugular vein and internal carotid artery above it. False aneurysm in artery.

no radial pulse could be felt. The wound healed without any difficulty and the patient was discharged 13 days postoperative.

Subsequent Course—This patient has been followed at various intervals since the operation. On March 23, 1937, there was no paralysis of the arm or any impairment of sensation. There was very slight weakness. All of the nerves seemed to have completely recovered their function.

The last examination was made in January, 1938, at which time there was no impairment of function or sensation in her arm or hand. The arm was not swollen. The interosseal muscles of the hand had not returned completely to their normal size, although there was no disability in the use of these muscles.

Case 23—Cincinnati General Hospital No. 63741. The patient, a colored man, age 53, was admitted first to the hospital August 12, 1933, suffering from multiple gunshot wounds of the left chest and one at the angle of the left jaw. Associated with this wound in the neck there was a large hematoma which in the course of about three days developed the typical characteristics of an arteriovenous aneurysm. A roentgenologic examination showed the bullet lying in the soft parts of the neck just to the left of the

midline. In its course it had penetrated the angle of the jaw but the fracture did not extend entirely through the mandible. The size of the heart was carefully noted by means of a teleoroentgenogram. The gunshot wounds healed without complications and the patient was discharged September 30, 1933. It was our plan to postpone the operation for two reasons. First, to allow an adequate time for the development of collateral circulation, and second, to see if the fistula would close spontaneously. The patient was

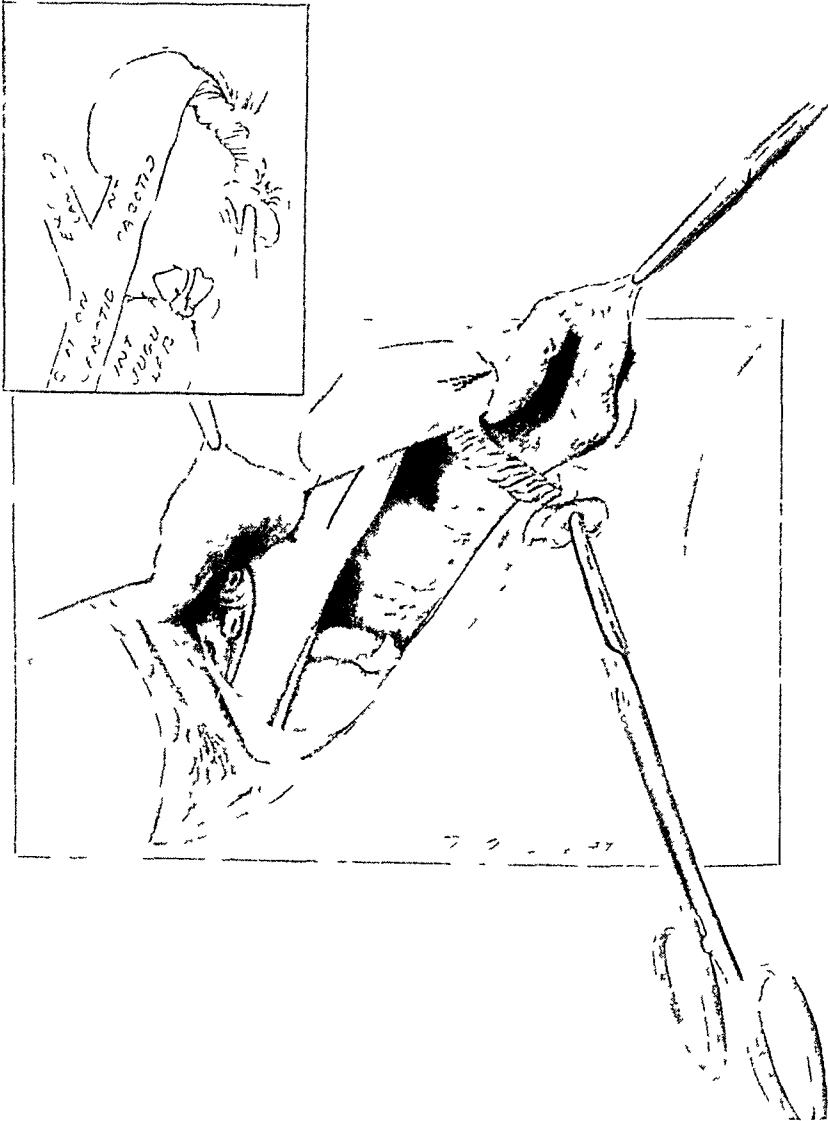


FIG 13—Case 23 Jugular vein divided and being twisted up so as to occlude arteriovenous fistula

watched in the Out-Patient Clinic from the time of his discharge until his readmission, October 29, 1936. He consented to come in at this time for operation because of increasing pulsation in his neck, ringing in the ear and spells of dizziness. During the two months preceding this admission, he had fallen backwards and to the left during these attacks of dizziness. In addition to these symptoms he had had some questionable difficulty in speaking and intermittent blurring of vision, associated with diplopia and an increased sweating of the left face.

At this time there was noted a swelling between the angle of the jaw and the lobe of the ear which was about the size of an egg. This was definitely pulsatile and ex-

hibited a very loud thrill and bruit. The bruit could be heard up as far as the temporal region and down the neck to the clavicle. There were no enlarged veins in the subcutaneous tissue of the neck or face. No weakness could be detected in the eye muscles. The fundi appeared to be normal. The patient complained of having double vision when he tried to look straight forward, in any of the lateral, superior or inferior directions he did not see double. There was no demonstrable weakness in the extremities of either side. Oscillometric readings were normal in all extremities. Venous pressure in the arm was 62 Mm. of water.

An electrocardiogram showed sinus tachycardia T_1 was diphasic and of low voltage. *Diagnosis* "Minimal evidence of myocardial disease." A roentgenogram of the skull, on this last admission, showed several metallic fragments in the neck, one of which was at

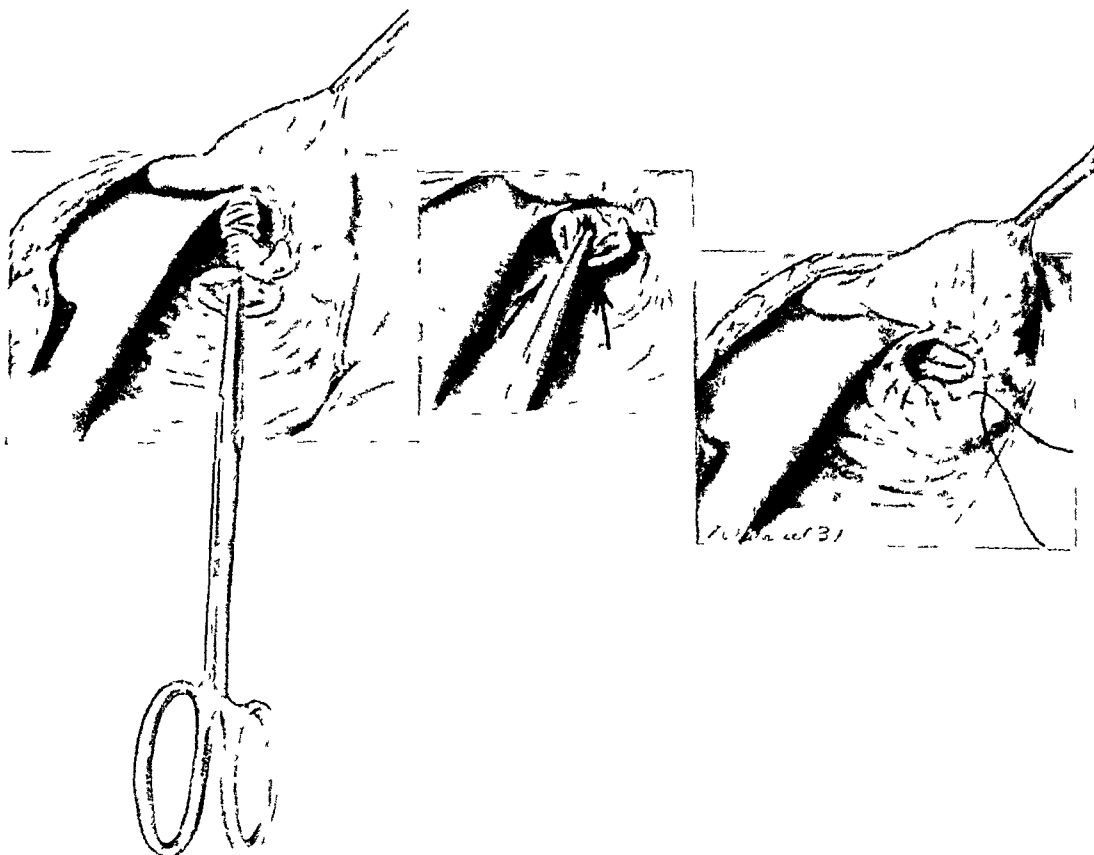


FIG. 14.—Case 23. Jugular vein twisted, pushed into jugular foramen and anchored so as to occlude the arteriovenous fistula.

the level of the second cervical vertebra. The bones of the skull were apparently normal. No demonstrable enlargement of the heart could be noted. Branham's bradycardic phenomenon was not demonstrable. Blood pressure in both arms before the operation was 124/86.

Operation—November 6, 1934. Under local anesthesia, the carotid artery, its branches, the jugular vein and vagus nerve were carefully freed up to the level of the posterior belly of the digastric muscle. This dissection was rather tedious because there were some large branches of the jugular vein which had to be carefully dissected free, ligated and divided. The fistula was located just at the base of the skull, and in the artery opposite the fistula there was an aneurysmal dilatation about the size of an olive. This extended up to the foramen in the skull. Communication with the internal jugular vein was so near to the base of the skull that one could not possibly free the vein beyond this point. The internal carotid artery was quite tortuous and about twice its normal size. When the dissection was fairly well completed, it was possible to see the arterial



FIG 15—Case 23 Photograph of specimen removed at autopsy three years and eight months after operation. Fistula closed, arterial aneurysm healed

blood squirting into the jugular vein, forming whorls which were easily visible through the wall of the vein

The operator was never in quite such a quandary, it was obvious that the involved artery and vein could not be excised because it would be impossible to ligate the distal stumps of the excised vessels. For some time the internal carotid artery and jugular vein were compressed at the same time, this, of course, appeared to stop the thrill and bruit, but the patient after several minutes began to become dizzy and showed obvious cerebral anemia. This convinced the operator that it would be necessary to try, at all hazards, to preserve the continuity of the internal carotid artery. The fistulous connection was so high that it could not be isolated enough to ligate it, neither could sutures be placed directly through the wall of the vein at this point. Finally, the jugular vein was divided low in the neck and the distal portion twisted until it definitely occluded the arteriovenous communication (Figs 12, 13 and 14). After this, the twisted jugular vein was pushed forcibly

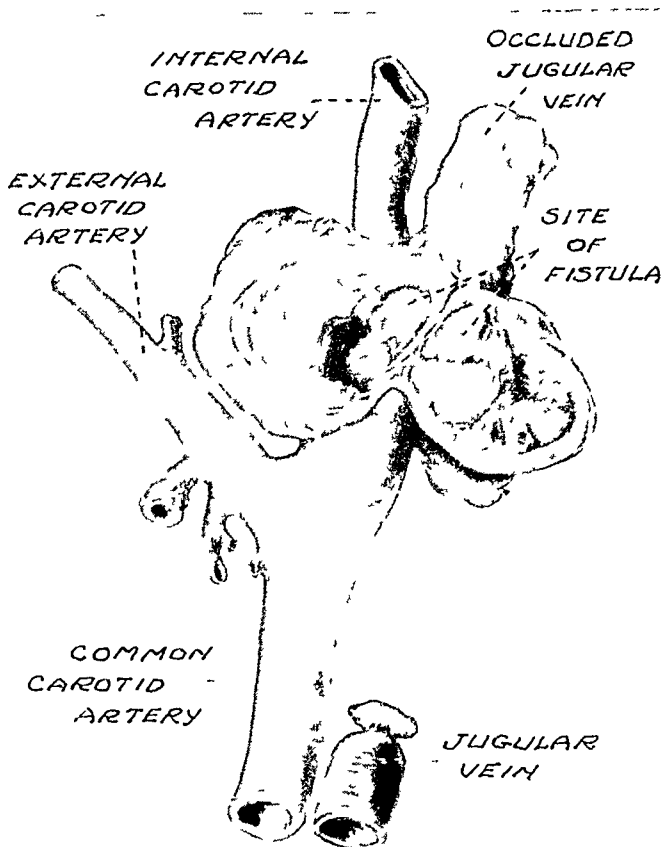


FIG 16—Case 23 Illustration of specimen removed at autopsy, with flap of healed arterial aneurysm turned back, showing site of fistula and restored lumen of the internal carotid artery

up toward the jugular foramen of the skull and held in this position by means of anchoring sutures, and a purse string suture, which caught some of the parotid gland and the fascia

in the bed of the jugular vein. This kept the twisted segment of vein from untwisting and kept it in position to block the communication. At the completion of the operation, and before closure of the wound, no bruit could be detected by means of a sterilized stethoscope. The wound was closed with interrupted, fine silk sutures.

It was interesting to note the fluctuations of the blood pressure during the course of the operation. The operation was begun at 8:40. About one-half hour later, when the carotid sinus was being carefully dissected, there was a noticeable rise in the blood pressure, reaching a peak of 160/110. The pressure when the operation was begun was 120/100. The elevated blood pressure was maintained for about one and one-half hours and then gradually dropped down to a little bit below what it had been during the manipulation. It was a very good clinical illustration of the rise in blood pressure during the manipulation of the carotid sinus. The operation required about three hours. At 1:00 P.M., about one hour after the operation, the blood pressure had gone back up to 170/110. It was still at this level at ten o'clock on the evening of the operation. By 9:30 o'clock of the next morning the blood pressure had dropped to 85/60, at 11:30 it was 94/64. On November 8, it was 120/80. On the ninth, it was 135/80, and on the succeeding days, up to the time of the patient's discharge from the hospital, November 18, 1936, it ranged around 135/95.

Follow-Up—When this patient was seen in the Follow-Up Clinic, January 20, 1937, there was no evidence of any arteriovenous communication. The patient's symptoms had practically disappeared. His only discomfort was a slight annoyance due to the division of the twelfth nerve at the time of operation. It was necessary to sacrifice this nerve in order to free the vessels sufficiently far up toward the communication.

The patient was sent for, February 1, 1938, for a follow-up study, and it was found that he was suffering from extensive bilateral pulmonary tuberculosis. He was admitted to the hospital and died from his tuberculosis about two weeks later. The autopsy showed that the fistula was completely healed and that the false aneurysm of the artery was filled with rather firmly organized blood clot. Through this clot the artery had assumed more or less its normal size. The vein distal to the fistula was also occluded (Figs. 15 and 16).

Case 29—Cincinnati General Hospital No. 80815. The patient, white, male, age 18, was admitted to the hospital October 10, 1937, with a gunshot wound of the right popliteal space. The bullet entered approximately the middle of this space and came out in the anterior part of the lower leg at about the junction of its upper and middle thirds. There was a considerable hematoma, but no serious external bleeding. Within 24 hours the presence of an arteriovenous aneurysm was evident from the characteristic thrill and bruit. The patient was kept in the hospital for 18 days, during which time the wound healed without infection, careful observations were made upon the heart and peripheral circulation. At the time of his discharge no pulse could be felt in the right foot, but the circulation seemed to be adequate. No nerve injuries were noted on admission, nor had any developed before he left the hospital. He was sent home to wait for the development of an adequate collateral circulation and the absorption of the hematoma before considering any curative surgical procedures.

He was seen again in the Follow-Up Clinic December 19, 1937, with no special complaints except a tendency of the right leg to become cold. At that time no pulses could be felt in the right foot. The hematoma had become largely absorbed and the tissues of the popliteal space were becoming soft. The signs of the fistula were more evident and there were no evidences of cardiac disability.

He was seen again January 23, 1938, when practically the same observations were made. At this time he complained of a little pain in the right knee joint after using his leg for a considerable time.

By February 10, 1938, it was felt that there was sufficient collateral circulation to undertake a curative operation. Besides, the studies of the leg showed that the proximal artery was definitely dilated. This was confirmed both by palpation and oscillometric studies. Average pulse, 65, average blood pressure, 100/64. No pulse could be felt below the knee. On numerous observations the patient exhibited the typical Branham's bradycardic phenomenon, the average drop in pulse rate on closure of the fistula being nine beats. On a few observations there were no striking changes in the blood pressure.



FIG. 17—Case 29—Popliteal arteriovenous aneurysm. Large false arterial aneurysm opposite fistula and extending anteriorly. Communication is with only one branch of the popliteal vein which divided high.

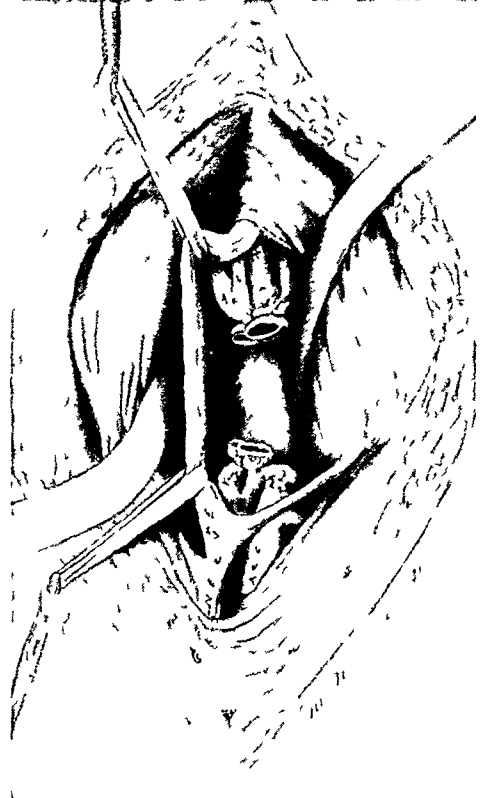


FIG. 18—Case 29. Complete extirpation of the involved popliteal vessels.

after occluding the fistula. There were no noticeable changes in the general venous pressure following occlusion of the fistula. In the left femoral vein it was $4\frac{3}{4}$ cm. of water when the fistula was open and the same when it was occluded. In the right femoral vein it was $5\frac{3}{4}$ cm. of water with the fistula open and $4\frac{1}{2}$ cm. when it was occluded. In the right and left antecubital vein the venous pressure remained about 10 cm. of water with the fistula open or closed. The circulation time in the right femoral vein averaged, with the fistula open, 13.6 seconds, with it closed, 17.3 seconds. The circulation time in the left femoral vein, with the fistula closed, was 14.6 seconds and 15.1 seconds with it open. The circulation time as measured in the left antecubital vein was 16.8 seconds when the fistula was open. Roentgenologic studies did not demonstrate any appreciable enlargement of the heart. On fluoroscopy, the pulmonary conus was moderately prominent with unusually vigorous pulsations. The heart became approximately one-quarter smaller with occlusion. The blood volume was 5,200 cc. October 28, 1937, and on February 12, 1938, it was 4,900 cc.

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Operation—February 16, 1938 Ether anesthesia The patient was placed on his abdomen and put in the Trendelenburg position so that the right leg would be well above the level of his heart The operation consisted of excision of the femoral artery and vein The fistula was located about one-half inch above the bifurcation of the femoral artery At this point the femoral vein was already divided into two vena comites The fistula communicated with only one of these In the artery opposite the fistula there was a false arteriovenous aneurysm about the size of an English walnut This projected directly anteriorly The operative procedure is illustrated in Figures 17 and 18 The operation was rendered rather difficult because of the danger of injuring the nerves, also, because of the fact that the vessels could not be very well delivered, as they were tied down by the anterior tibial branches of the femoral artery The large vessels were ligated with double braided silk, the smaller vessels with very fine silk The proximal artery was definitely dilated to about half again its normal size

The knee was completely immobilized by a crinoline encasement On the following morning good pulses could be easily detected in both the dorsalis pedis and posterior tibial vessels These have remained good, although the volume has lessened somewhat since about the third day postoperative

Three weeks after operation the pulse was 48, blood pressure, 102/60, and blood volume, 5,300 cc In the right and left arms and right femoral vein, the venous pressure was 7.75 cm of H₂O The circulation time in the right femoral vein was 17.6 seconds In the right arm the circulation time was 19.6 seconds

Case 25—Cincinnati General Hospital No 73338 The patient, white, male, age 19, was admitted to the hospital April 16, 1937, because of a pulsating mass below and behind the right ear This was not causing any trouble, except that he wished to have it removed in order to be made eligible for admission into the U S Navy He had previously been in the hospital in September, 1936, for the repair of a left, indirect inguinal hernia It was not noted at that time that he had a cirroid aneurysm of his neck The lesion had evidently grown considerably between that admission and the one of April, 1937 The patient believed that there had been something wrong with the blood vessels in his neck since infancy There was no history of any injury It in no way incapacitated him, but he was becoming more and more conscious of a roaring noise in the right ear, especially when lying down He had engaged in strenuous work and athletics without any evidences of cardiac disability

Just behind and below the right ear there was a visible pulsation, over which one could feel a strong thrill and on auscultation hear a loud and typical to-and-fro arteriovenous bruit The carotid artery on this side appeared to be definitely enlarged Compression of it caused the bruit to disappear and the swelling to collapse The external jugular vein was much enlarged and carried a strong bruit Firm pressure directly below the tip of the ear made this bruit almost disappear When the patient bent his head forward the swelling became definitely larger and he occasionally felt a slight numb sensation in the region of the ear However, none of the nerves were apparently involved

A teleroentgenogram of the heart showed no enlargement Blood pressure in the right arm averaged 120/60, and in the left arm, 100/50 Neither blood pressure was noticeably affected by occluding the fistula The pulse was 70 and it was not slowed by pressure over the aneurysm Venous pressures in the right arm were 12.5 cm of water, and in the left, 11 cm Circulation time in the left arm was 16.4 seconds Blood volume, 6,950 cc

Operation—May 4, 1937 (Figs 19, 20, 21 and 22) Local anesthesia In the process of dissection the digastric and stylohyoid muscles, the posterior occipital, external, internal and the common carotid vessels, the hypoglossal nerve and the lower margin of the parotid gland were all exposed Occlusion of the external jugular vein at a point low in the neck caused rapid dilatation distal to the occlusion, and through the wall of the

vein arterial blood could be seen swirling from the force of the arterial communications. Occlusion of the external carotid artery stopped the swirling, the bruit and the thrill

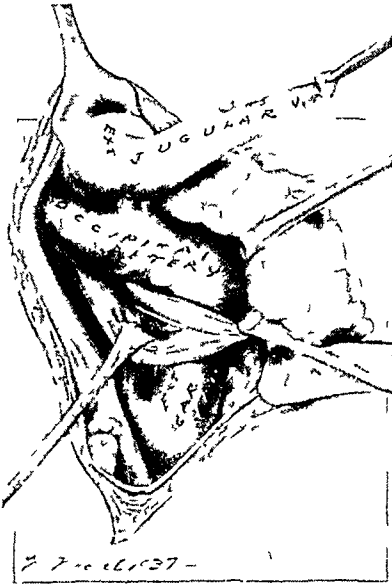


FIG 19—Case 25 External jugular vein divided and held up showing communications with the huge occipital artery. External carotid is also very large

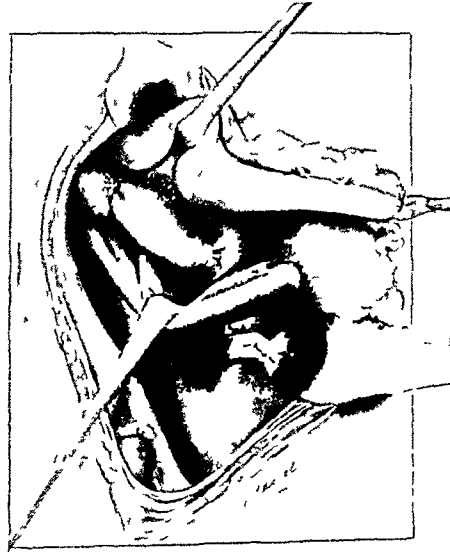


FIG 20—Case 25 Two ligatures on the occipital artery, one on the external carotid. Ligation of three definite arteriovenous communications

Occlusion of the internal carotid artery did not affect it. The external carotid artery was noticeably dilated, measuring 1.4 cm in diameter, while the internal carotid artery measured only 0.8 cm in diameter. The posterior occipital artery was tremendously enlarged,



FIG 21—Case 25 Twisting of the external jugular vein to occlude any other fistula which may be higher

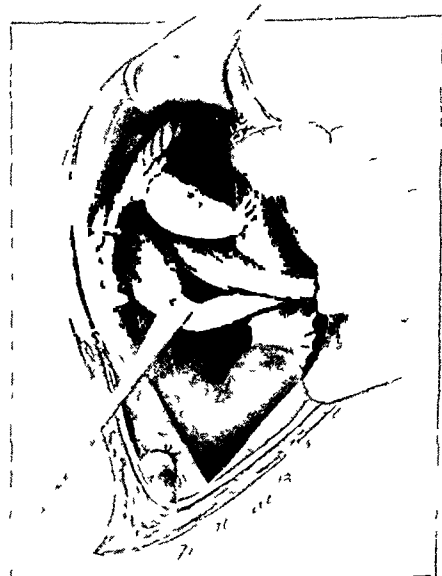


FIG 22—Case 25 Twisted external jugular vein anchored to the sternomastoid muscle, in order to prevent its untwisting

measuring 0.9 cm in diameter. During the process of freeing the bifurcation of the common carotid artery, the pulse dropped from 100 to 80.

The occipital artery was ligated twice with braided silk, first, at its point of disappearance behind the parotid gland and again at the point of its origin from the carotid

artery The external carotid artery was ligated with heavy tape just above its origin from the common carotid

The external jugular vein was then freed low in the neck and divided It was dissected upward to the point of its disappearance deep in the parotid gland In this region numerous vessels communicating with the occipital artery were encountered As these communicating vessels were ligated, activity within the vein became less, but not until one high up in the neck, approximately one-quarter inch in diameter, was ligated did the vein collapse and all activity stop At this time, no bruit could be heard through a sterile stethoscope The patient said that the noises in his head, to which he had become accustomed, had ceased

In order to obliterate any other communications which might not have been discovered, the long segment of external jugular vein was twisted until it became a very small cord This was anchored to the sternomastoid muscle in such a way that it could not untwist Closure was then made with interrupted, fine silk sutures Following the operation there was no noticeable change in the pulse rate This patient has been seen on numerous occasions since the operation, the last time being February 5, 1938, at which time there was no evidence of any recurrence of the cirsoïd aneurysm

Immediately after the operation, the blood pressure in the left arm was 140/25, this was at 1 00 P M By 11 00 P M the blood pressure was 120/60 On the following day, it was 110/65, and thereafter it ranged around 115/60 This fluctuation in blood pressure immediately after operation was no doubt connected with manipulation of the carotid sinus On February 9, 1938, the venous pressure was 115 cm of water in the right arm Circulation time in the left arm was 12.4 seconds, in the right arm, 12 seconds

Blood volume on May 15, 1937, was 5,670 cc, and on February 9, 1938, was 6,430 cc

Case 28—Cincinnati General Hospital No 81335 The patient, white, male, age 16, was admitted to the hospital October 22, 1937 On October 3, 1937, a pistol shell exploded and a small fragment of it hit the inner side of his right upper arm about three inches above the elbow He bled profusely, losing about a pint of blood, until he received first aid On the day following this accident, the upper arm became markedly swollen, this continued for three days and then gradually began to subside With the subsidence of this swelling a small pulsating tumor appeared at the site of the injury, over which a thrill and bruit were noted The swelling continued to increase rapidly and the skin over it became very thin, he also developed a weakness in the gripping of his hand, and a tingling sensation and an inability to use his hand well The pain at the site of the injury became increasingly severe

Physical Examination—At the time of admission to the hospital he had an extensive, though not complete, paralysis of the median nerve and severe causalgia in the forearm and hand The swelling above the elbow (Fig 23) measured about 4 cm in



FIG 23—Case 28 Arteriovenous aneurysm of brachial vessels Skin near rupturing Rapidly progressing paralysis of median nerve Operation 23 days after injury by a piece of steel

diameter The skin at the site of the puncture wound was very thin and there was real danger of spontaneous rupture Over this swelling a thrill and bruit, characteristic of arteriovenous aneurysm, were very pronounced Radial pulse could be felt, though markedly lessened The blood pressures were the same—120/60 in both arms Pulse

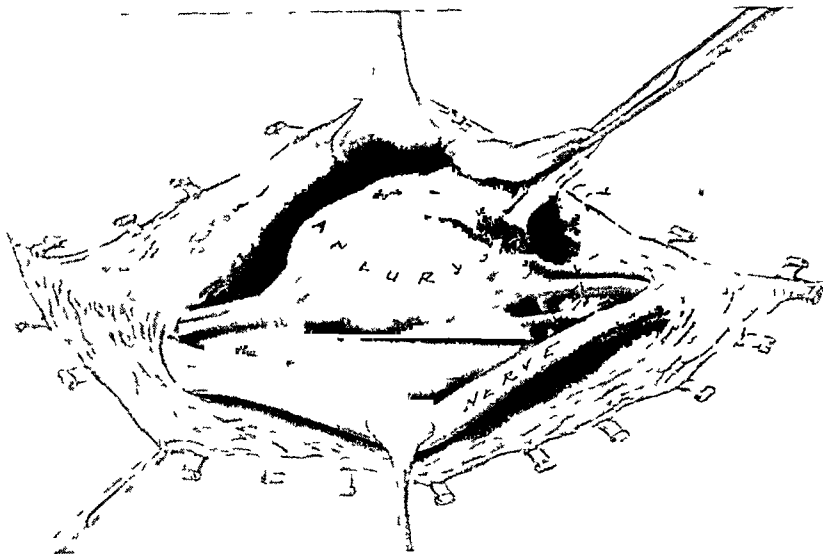


FIG 24—Case 28 Nerve retracted from its bed in aneurysm, where pressure was causing paralysis Some very thin skin being excised with the aneurysm Skin is protected by towels clipped to its edges

80, and did not slow down on occluding the aneurysm, but the diastolic pressure rose 30 Mm Hg Venous pressure before operation was 9 cm of water in the left arm and 10½ cm of water in the right arm Circulation time, as determined by the NaCN method, was 21 30 seconds in the left arm, and 14 0 seconds in the right arm, proximal

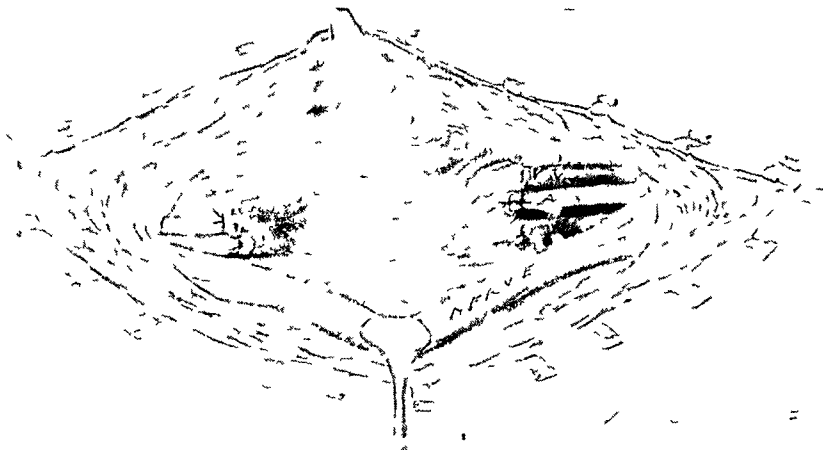


FIG 25—Case 28 Aneurysm completely excised Vessels ligated with silk

to the fistula The heart was normal in size An electrocardiogram was normal Due to the progressive median nerve palsy, the severe causalgia and the danger of rupture of the aneurysm, immediate operation was decided upon

Operation—October 26, 1937 (Figs 24, 25 and 26) Both of the vena comites communicated with the divided artery Both the proximal and distal ends of all vessels involved were patent The aneurysm was completely excised The median nerve was stretched over the aneurysmal sac and definitely flattened It had not been injured by the fragment of shell, but was obviously being damaged by the pressure and pulsations of

the aneurysm Following operation there were no complications and no appreciable embarrassment to the circulation of his hand and forearm The pulse and temperature remained normal He was discharged November 4, 1937 Blood pressure 100/70, venous pressure left arm, 8 cm of water, circulation time left arm, 20 seconds

Follow-Up—January 9, 1938 Sensation and muscle power had all returned to normal A faint radial pulse could be felt

Case 27—Christ Hospital No 112543 The patient, white, male, age 33, height 6 feet, weight 156 pounds, was admitted to the hospital, September 8, 1937, with the diagnosis of an aneurysm of left arm He had consulted a physician because of nervous spells, vague gastro-intestinal complaints, and shortness of breath on exertion These symptoms had gradually increased during the past six months There was found on further questioning that in association with the shortness of breath, there was palpitation, but no precordial pain and no edema of ankles Examination revealed an arteriovenous fistula of the left arm which it was thought explained many of the symptoms The fistula had evidently developed 16 years before, at the age of 17, at which time he sustained a compound fracture of the left humerus just above the elbow This was reduced and placed in a plaster encasement for several days, after which a secondary reduction was undertaken When the encasement was removed some time later, he was told he had an aneurysm, which was subsequently operated upon The patient does not recall whether his arm was swollen, what the condition of the circulation in the fingers was or when the operation was performed He does, however, remember being told that at the operation he had nearly died from loss of blood, and that it would be dangerous for him to be operated upon again, and that if he were careful, he would not have any trouble He therefore refrained from athletic sports and never considered having the fistula operated upon

Physical Examination—The general examination was essentially negative The patient was tall and thin, and somewhat nervous There was no evidence of cardiac decompensation There was some deformity of the left arm due to the old fracture, with some loss of the carrying angle There was a large, broad scar on the cubital region extending up the inside of the arm Underneath this scar was a visible, pulsating mass with the typical thrill and bruit of an arteriovenous fistula The brachial artery entering it was quite large and felt about 1 cm in diameter There was no dilatation of the peripheral veins, leading to the surmise that the vein distal to the fistula had been ligated, a fact subsequently confirmed at operation There was a very weak pulsation felt in the left radial artery, and the circulation in the fingers was good Obliteration of the fistula by pressure directly over it caused the pulse to drop from 88 to 60 within one minute Percussion of the heart indicated that it was moderately enlarged, but the teloroentgenogram did not reveal any enlargement Without occlusion of the aneurysm, the blood pressure in the right arm was 100/70, with occlusion of the aneurysm it was 125/85 Blood pressure in the left arm was 130 systolic, murmur was not heard until 110, maximal at 95 Circulation time, right antecubital vein, with 0.35 cc NaCN, was 15 seconds without occlusion Venous pressure right antecubital vein without occlusion of fistula was 8.5 cm H₂O, with occlusion, 8.5 cm H₂O Blood volume 5,400 cc, 8.17

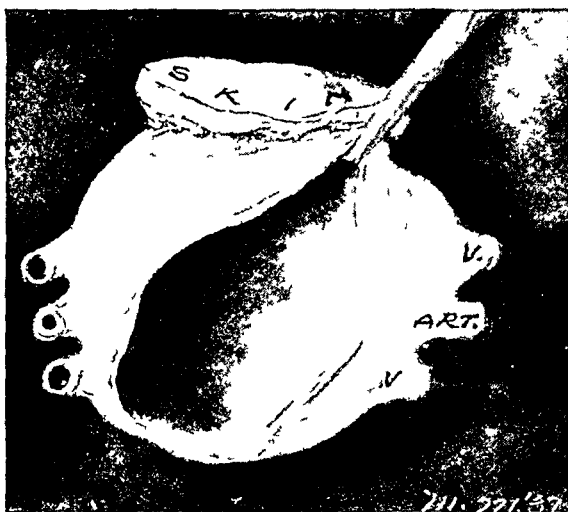


FIG 26—Case 28 Window cut in the side of aneurysmal sac Both veins and the artery were divided and communicated from within the false aneurysmal sac

per cent body weight Hematocrit, 43.2 per cent Plasma volume, 3,060 cc, 4.53 per cent body weight The electrocardiogram was normal

Operation—September 11, 1937 The brachial artery was about 1 cm in diameter proximal to the fistula The vein, proximal to it, about 1.5 cm in diameter The

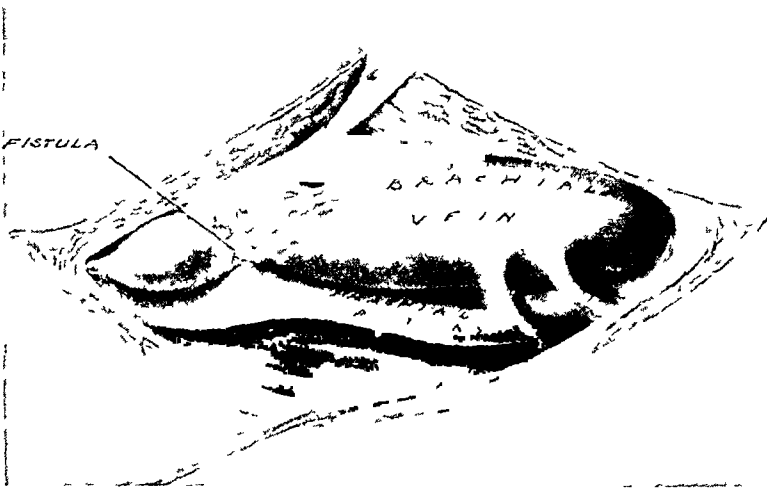


FIG 27—Case 27 Arteriovenous aneurysm of brachial vessels, duration, 16 years
Vein distal to fistula, ligated over 15 years ago

vein, distal to the fistula, was a thin fibrous cord, and had apparently been ligated previously The artery distal to the fistula, was about 7 to 8 Mm in diameter Occlusion of the artery, proximal to the fistula, reduced the blood flow through the fistula approximately 60 per cent, but occlusion of the distal artery was necessary to stop the flow The artery, proximal and distal to the fistula, was ligated with one-half inch tape, the

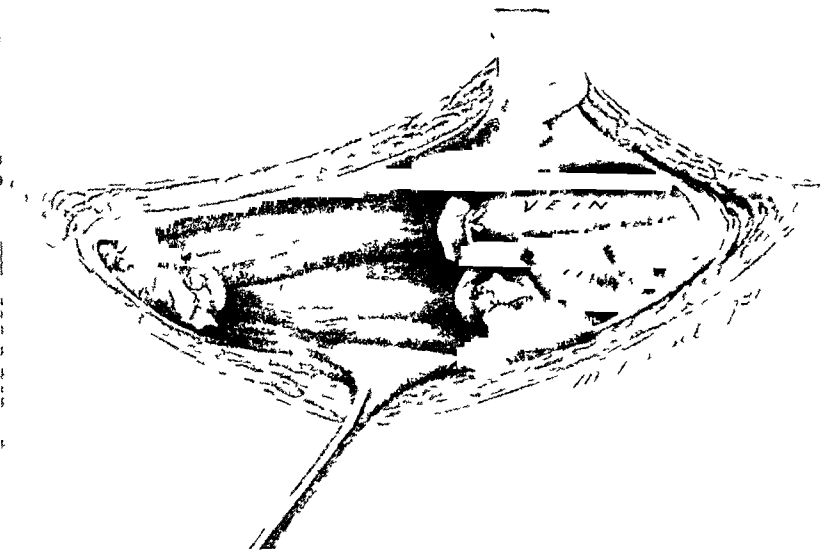


FIG 28—Case 27 Operation as completed

vein, proximal, with braided silk, the small vein, distal, with medium silk, the fistula-bearing vessels were excised (Figs 27 and 28) There was a good pulse at the left wrist immediately after operation

Subsequent Course—Thirteen days postoperative Blood pressure, right arm, was 115/75, pulse, 80, circulation time, 19.5 seconds, venous pressure, 10 cm of water, blood volume, 4,800 cc, 7.2 per cent body weight, hematocrit, 42.25 per cent, plasma

volume, 2,760 cc, 4 per cent body weight On September 30, 1937, the teleoroentgenogram showed no change On December 20, 1937, the heart had become slightly smaller, and all of the patient's former complaints had disappeared The brachial artery had become much decreased in size

Case 21—Cincinnati General Hospital No 56203 The patient was admitted to the hospital March 9, 1936, with a left subclavian arteriovenous aneurysm He had previously been in this hospital, in December, 1933, with advanced tuberculosis of both apices The aneurysm had resulted from a gunshot wound with a 22 caliber bullet, March 22, 1935 Following this injury there was mild shock but very little bleeding Shortly after, the patient noticed that his left arm was partially paralyzed and that he had a peculiar noise in the region of the left shoulder He said that it sounded like the exhaust of steam The motion and sensation in the left arm gradually improved up to the time the patient was first sent into the hospital for careful studies Blood pressure, 126/60, venous pressure, in the right arm, 5.2 cm water, while in the left arm, the venous pressure was 9 cm water Circulation time in the left arm, 15 seconds A teleoroentgenogram showed a slight dilatation of the aorta The paralysis in his arm involved primarily the ulnar nerve, but this was not complete Due to the patient's extensive pulmonary tuberculosis, the positive Wassermann, and the absence of any serious cardiac damage, it was decided to postpone any operative procedure The patient was discharged after five days' study and told to rest as much as possible because of his tuberculosis

He was readmitted, May 13, 1936, for a period of 12 days for further study For the past year he had been taking much rest at home At this time it was noted that all signs of a communication between the artery and vein had disappeared There was a faint systolic bruit, probably due to the variation in the size of the artery, but no evidence whatever of a characteristic to-and-fro arteriovenous murmur Apparently the fistula had closed spontaneously, as a result of the patient's rest in bed On several occasions subsequently, this patient has been seen, but showed no evidence of an arteriovenous fistula

Case 4—Children's Hospital No 2356 The patient, white, male, age 8, was admitted to the Children's Hospital, March 12, 1928, with an eye condition for which he had previously consulted Dr D T Vail, Jr In June, 1927, eight months previously, the child had injured his left eye by running a small piece of chicken wire into the eyeball This puncture was apparently into the lower inner quadrant of the eye, although no scar of it could be detected Six weeks later the eye became reddish and he was treated for pink-eye By September, 1927, the left eyelids, particularly the upper lid, were noted to be swollen, and the conjunctival veins had become very large and very red Later, the supra-orbital vein became large, and varicosities appeared in the eyelids and on the nose around the inner canthus of the eye When he was first seen by Doctor Vail, a few days before our operation, an aneurysm of the eye was detected The conjunctival veins were very large and distended with arterial blood They, as well as the larger varicosities of the eyelids, nose and forehead, definitely pulsated There was no edema, which is usually very marked when there is an intracranial arteriovenous fistula between the cavernous sinus and internal carotid artery The retinal veins were distended and pulsated Vision did not appear to be disturbed On light palpation over the closed eye, a faint thrill could be felt A definite arteriovenous bruit could be heard over the eye, nose and forehead Temporary occlusion of the common carotid artery caused the eye to recede, the veins to collapse partially and to cease pulsating, and the thrill and bruit to disappear Not knowing exactly where the perforation had occurred, and because the most marked signs of the cirsoid aneurysm were at the inner angle of the eye, it was thought that the abnormal communications were probably between branches of the external carotid artery and the neighboring veins

Operation—March 13, 1928 The bifurcation of the common carotid artery was first

exposed Here we were surprised to find that temporary occlusion of the external carotid artery had no effect on the aneurysm but that occlusion of the internal carotid completely stilled it Consequently, the external carotid artery was permanently ligated with a heavy silk ligature, and the common carotid was occluded by a removable aluminum band Through a Killian incision over the left tear sac and extending into the brow, the supra-orbital and other large veins in the exposed area were excised Another small incision in the upper eyelid allowed the removal of a large vein All ligations were made with silk ligatures

Subsequent Course—For five days after the operation, the patient vomited very frequently On the third day a slight weakness of the right face and of the right arm was noted This paralysis did not progress, and disappeared entirely in about two weeks We interpreted the vomiting, as well as the paralysis, as being due to cerebral anemia During this period of uneasiness, it was a great comfort to know that we could remove the metallic band if the symptoms demanded it

September 27, 1930 Examination showed that the dilated conjunctival veins had almost completely disappeared There was no exophthalmos No enlarged veins in the eyelids, about the nose or on the forehead were seen Auscultation over and about the eye revealed no bruit There was no evidence of any right-sided weakness Mental development appeared to be normal

In the neck, the left common carotid artery was about one-quarter as large as the right, and definitely pulsated At the site of the occluding band, a loud, harsh systolic bruit could be heard such as one can hear when an artery is markedly constricted Four months after the original operation, the artery was apparently totally occluded, as neither a murmur nor a pulsation could be detected Since that time, and now, there has been a partial restoration of the lumen with a return of function in the artery

April 13, 1938 Both eyes appeared to be normal Vision and muscular action were undisturbed Retinal vessels did not pulsate and have returned to normal size The fistula remained closed No thrill or bruit was demonstrable either over or about the eye

The band could not definitely be felt The left carotid artery was of normal size and compression of it caused a good temporal pulse to disappear Compression of the right common carotid artery did not affect the left temporal pulse The artery, just distal to the band, was not demonstrably enlarged A soft systolic bruit, indicating only a mild constriction, could be heard over the site of the band Evidently the lumen of the artery at the site of the band has been restored almost to normal size

Case 30—Cincinnati General Hospital No 88134 The patient, white, male, age 19, was admitted to the hospital, February 9, 1938 He had four cirroid aneurysms (Fig 29)—one in the neck, two in the left forearm and one on the dorsum of the left foot All of them appeared spontaneously The two on his left forearm appeared about ten or 12 years ago without any antecedent injury, so far as he knew They increased slowly in size, except during the past year or two, when he did not note any particular change Three weeks before admission the smaller of these two lesions on the left forearm, the one situated just above the wrist, was excised by Dr George Curtis of Columbus, Ohio He reported the lesion removed as being an arteriovenous aneurysm

The next lesion to appear was in the left side of his neck The patient first observed this about three or four years ago It grew rapidly and recently interfered somewhat with his voice, which frequently became "husky"

The lesion on the dorsum of the left foot was noted about the same time as the lesion in his neck However, it had not grown nearly so rapidly

None of these lesions ever caused the patient any pain He continued to work hard and did not note any increase in shortness of breath or forcible heart action There was never any swelling of his ankles The patient at no time was conscious of any noise connected with the tumors

Physical Examination—The patient's face was slightly congested, which condition

the patient himself had been conscious of In the left side of his neck, extending across the midline to the right side, there was a very large pulsating mass, which presented irregularities due to obvious large blood vessels beneath the skin The skin was not telangiectatic and appeared to be normal It moved freely over the lesion The size and extent of this lesion are well depicted in Figure 29

On palpation, there was a very pronounced thrill over the entire surface of the swelling, most marked over the lateral margin of the sternomastoid muscle All of the vessels pulsated very forcibly, especially an extremely large one just below the left submaxillary gland The bruit was very loud, particularly at the point where the thrill was most easily felt This bruit was transmitted up into both temporal vessels Curiously enough, it was a little more pronounced on listening over the right temporal



FIG. 29.—Case 30. Patient with four spontaneous cirroid aneurysms. A very large one in the neck, a small one in the left foot, and two in the left forearm (lower tumor of arm removed elsewhere, three weeks before). All lesions, especially that in the neck, pulsated vigorously, and exhibited the typical thrills and bruits of arteriovenous aneurysms.

artery The lesion did not seem to extend below the level of the clavicle or far up under the jaws On compressing the carotid artery on the left side the thrill could be made to disappear, but there remained a faint bruit On compressing both carotid arteries the bruit became almost inaudible One could not detect any definite increase in the size of either carotid artery When the patient bent forward, his face became rather quickly and markedly flushed, almost cyanotic

On the volar surface of the left forearm there was another pulsating tumor, the center of which was situated about 8 cm below the internal condyle of the humerus The size of this tumor was roughly that of a large English walnut Its vertical diameter was 5.5 cm, the transverse diameter about 5 cm This tumor pulsated and presented an irregular contour, due obviously to blood vessels beneath the surface of the skin The skin, however, was normal and moved freely over the swelling The color of this lesion was slightly bluish, due unquestionably to the blood in the vessels beneath

the skin. A faint thrill could be felt over this tumor, there was a very definite and typical arteriovenous bruit. The bruit and thrill could be made to disappear by occluding the brachial artery, which appeared, on palpation, to be about normal in size.

Farther down in the forearm there was a recent wound which measured about 7 cm. This was the site of the operation three weeks ago. The radial and ulnar vessels appeared to be normal. A tumor, quite similar to the one described in the forearm, only about one-quarter the size, was situated on the dorsum of the foot. The skin over it was normal. It was not quite so irregular, but a characteristic arteriovenous bruit was audible over the mass. The pulsation and the bruit disappeared on compressing the femoral artery. The femoral artery appeared to be normal. This patient had definite cardiac enlargement and a slight systolic murmur at the apex.



FIG. 30.—Case 30. Dissection of the aneurysm from left forearm except for one large tortuous anastomosing artery. Before dividing this vessel the aneurysm pulsed and exhibited the signs of a cirroid.

Closure of the large communications in the neck by direct pressure caused a definite slowing in the heart rate of 20 beats, and the blood pressure in the right arm changed from 130/65 to 140/78.

First Operation—February 12, 1938. The cirroid aneurysms of the left arm and on the dorsum of his left foot were removed under local anesthesia. In the case of the arm it was easy to demonstrate two or three large arteries running directly into, and communicating with, the mass of blood vessels. It was possible to dissect the entire mass free except for the largest of these communicating arteries. The mass would still pulsate when the artery was open, but would cease on occluding it. Following the removal of the tumor, injection of this main artery with Hill's solution filled all the blood vessels in the mass (Fig. 30).

In the case of the foot there were two arteries close to the dorsalis pedis artery

ARTERIOVENOUS ANEURYSMS

which ran directly into the cirroid aneurysm (Fig 31) There was no direct communication with the dorsalis pedis Closure of these two communicating arteries stopped the activity of the aneurysm The excision of this tumor was relatively easy compared with that in the arm In both instances the ligations were made with silk and the wounds were closed with interrupted silk sutures without drainage

Following these two operations there was no noticeable change in the cardiovascular mechanism of this patient (Fig 32) The wounds healed without any difficulty

Second Operation—February 26 1938 (Figs 33, 34, 35, and 36) Ether anesthesia An attempt was made to do something to the huge cirroid aneurysm which involved both sides of the neck, especially the left An incision was made along the border of the sternomastoid muscle from the tip of the ear almost to the clavicle and then curved in front of the throat across the midline In the subcutaneous tissues countless small blood vessels were encountered and progress was necessarily very slow We were finally able, however, to expose the carotid artery and jugular vein from the clavicle up above the bifurcation of the common carotid artery The jugular vein was about three times its normal size Through its wall could be seen whirling arterial blood, and there was an actual tremor, which presented the thrill and the bruit which

were so pronounced before operation Low in the neck there were two large branches which connected the jugular vein with the huge vessels making up the cirroid aneurysm When these were divided the jugular vein immediately collapsed to about its normal size,

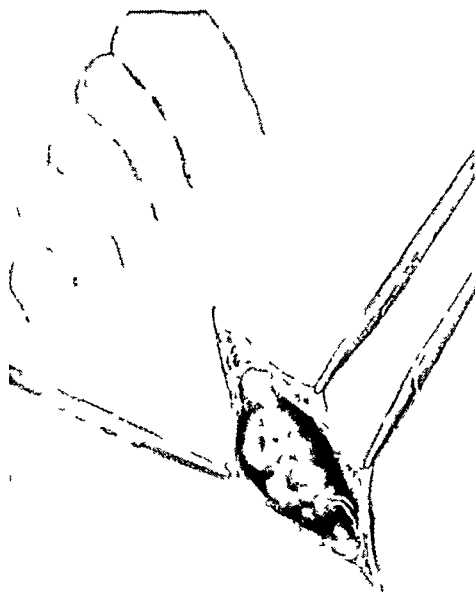


FIG 31—Case 30 Aneurysm of foot showing two distinct communicating vessels No direct connection with dorsalis pedis artery

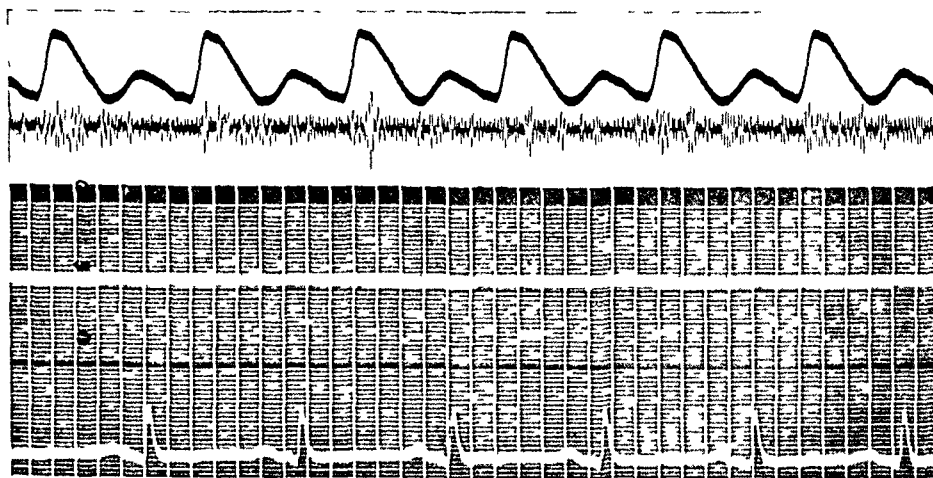


FIG 32—Case 30 Simultaneous electrocardiogram, radial pulse tracing, and sound tracing showing continuous murmur over carotid artery

the thrill and bruit disappeared from it and it was possible to detect a faint bruit only over the rest of the cirroid aneurysm, through a sterile stethoscope Following this procedure the bifurcation of the common carotid artery was carefully freed and, first, the superior thyroid artery was ligated This reduced the bruit, but did not make it disappear

entirely The external carotid and ascending pharyngeal arteries were then ligated, following which the huge cirroid aneurysm almost ceased to pulsate

The next procedure was to locate and ligate the inferior thyroid artery After doing this, the flap of skin and subcutaneous tissue were dissected off the surface of the aneurysm to the midline of the neck and up to a point above the hyoid bone Starting laterally an effort was made to remove most of this mass of blood vessels There was still some pulsation and the control of hemorrhage was a ticklish proposition It was soon possible to determine that the lower two-thirds of the thyroid gland was not involved

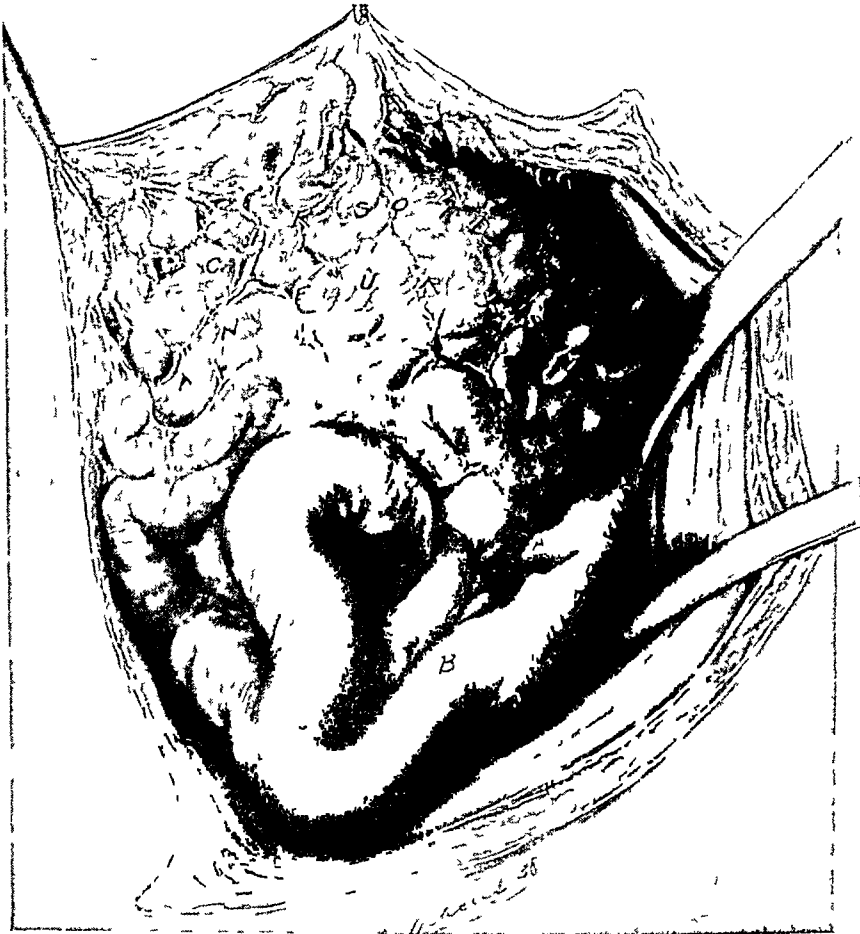


FIG 33—Case 30 A, B Two huge vessels from the cirroid aneurysm emptying arterial blood into the jugular vein

in the cirroid condition The upper one-third of the thyroid was markedly involved, and the condition extended behind the trachea on to the esophagus and far over to the right side of the neck The aneurysm extended also above the hyoid bone The dissection was continued until it was obvious that no more could be removed from this side without the danger of injuring the esophagus At this point, large transfixion sutures of braided silk were used to ligate the mass of vessels which had been largely freed On doing this, a rather large hole was torn in a big blood vessel just behind the trachea, at about the level of the upper third of the thyroid gland This was controlled by direct finger pressure until the operator secured a piece of muscle and plugged the hole by suturing it directly into the opening It was noted at this time that the bleeding was still very active After the hemorrhage had been controlled, the wound was closed with interrupted fine silk sutures, without drainage A plaster encasement was applied to the patient's neck and head to immobilize the wound Ligation of the right external carotid

artery was considered, but this was deferred until a later date because the operation had already consumed about four hours

Subsequent Course—Following this operation there was a little difficulty in swallowing and talking for two days, but otherwise the convalescence was quite uneventful. The wound healed per primam. The left vocal cord was not paralyzed. The blood pressure in both arms on admission and for eight days after the neck operation ranged around 155/80, on leaving the hospital it was 124/88. The patient was discharged, March 27, 1938, with a definite bruit still audible over the front of the neck, but no thrill or pulsa-



FIG 34—Case 30. A, B, Large connecting veins, from cirrroid to jugular vein divided. Superior thyroid, external carotid and ascending pharyngeal arteries divided.

tions could be felt. This bruit could be made inaudible by compression of the right common carotid artery at its bifurcation but not by compression lower down in the neck. Evidently the reversed circulation through the circle of Willis was enough to keep the cirrroid aneurysm active when only the common carotid artery was occluded.

Special studies of the heart in the Cardiac Laboratory showed: February 11, 1938. Circulation time right arm, 18 seconds, left arm, distal to the fistula, 21 seconds, left arm, proximal to the fistula, 11.6 seconds. Venous pressure, right arm, +8 cm of water, left arm, distal to the fistula, +12 cm, proximal, +7.5 cm. Blood volume, 5,440 cc. March 21, 1938. Circulation time in left arm was 12.2 seconds. Venous pressure right arm, 5 cm of water, left arm 5 cm. Blood volume, 5,070 cc.

Third Operation—April 26, 1938. Under local anesthesia, the right external carotid artery was ligated. This operation, together with the previous one, effected a complete sacrifice of both external carotid arteries, there still remains, however, a faint audible bruit.

Case 16—Holmes Hospital No 340334 An instance of a large arteriovenous hemangioma involving the right forearm and hand The patient, white, female, age 24, was admitted to the hospital June 18, 1934 The condition she presented was obviously congenital It was not, however, noted by the parents until she was about three years old, when there was observed some irregularity and a slight enlargement on the volar surface of the right forearm The condition gave the patient no trouble until about one year before admission, although the swelling had gradually increased in size During the year previous to admission, the swelling seemed to have increased rather rapidly and



FIG 35—Case 30 Ligatures placed preparatory to amputating a large portion of the cirroid aneurysm Note the involvement of the upper third of thyroid gland, and the extension of the cirroid aneurysm behind the trachea into the right side of neck Inferior thyroid artery is ligated

had begun to cause her considerable trouble, particularly a sensation of discomfort and tightness when the arm was held down, and a rather excessive fatigability of the fingers, with a definite impairment of their function

Physical Examination revealed an apparently healthy girl, except for the congenital vascular lesion involving the volar surface of the right forearm and hand (Fig 37) The swelling was rather irregular and increased perceptibly when the arm was held down There was definite diminution in the size when the arm was elevated If the middle of the forearm was squeezed when the arm was hanging down, a definite fluctuation wave could be felt in the palm of the hand, accompanied by an increase of the swelling in the palm In places there were light-bluish discolorations of the skin, but there was no definite involvement of the skin at any place by an angiomatous condition The super-

ficial veins were quite large. No thrill and no bruit could be demonstrated. The radial and ulnar vessels were easily palpable. Throughout the extent of this vascular lesion one could feel small, hard bodies, which were thought to be calcified phleboliths (Fig 38). The patient's blood pressure was essentially the same in both arms, namely, 105/78.

The patient had had so much trouble during the previous year that she had frequently been advised to have her arm amputated lest the growth would extend, rupture and cause fatal hemorrhage. With considerable hesitation, an operation to excise the lesion was undertaken.

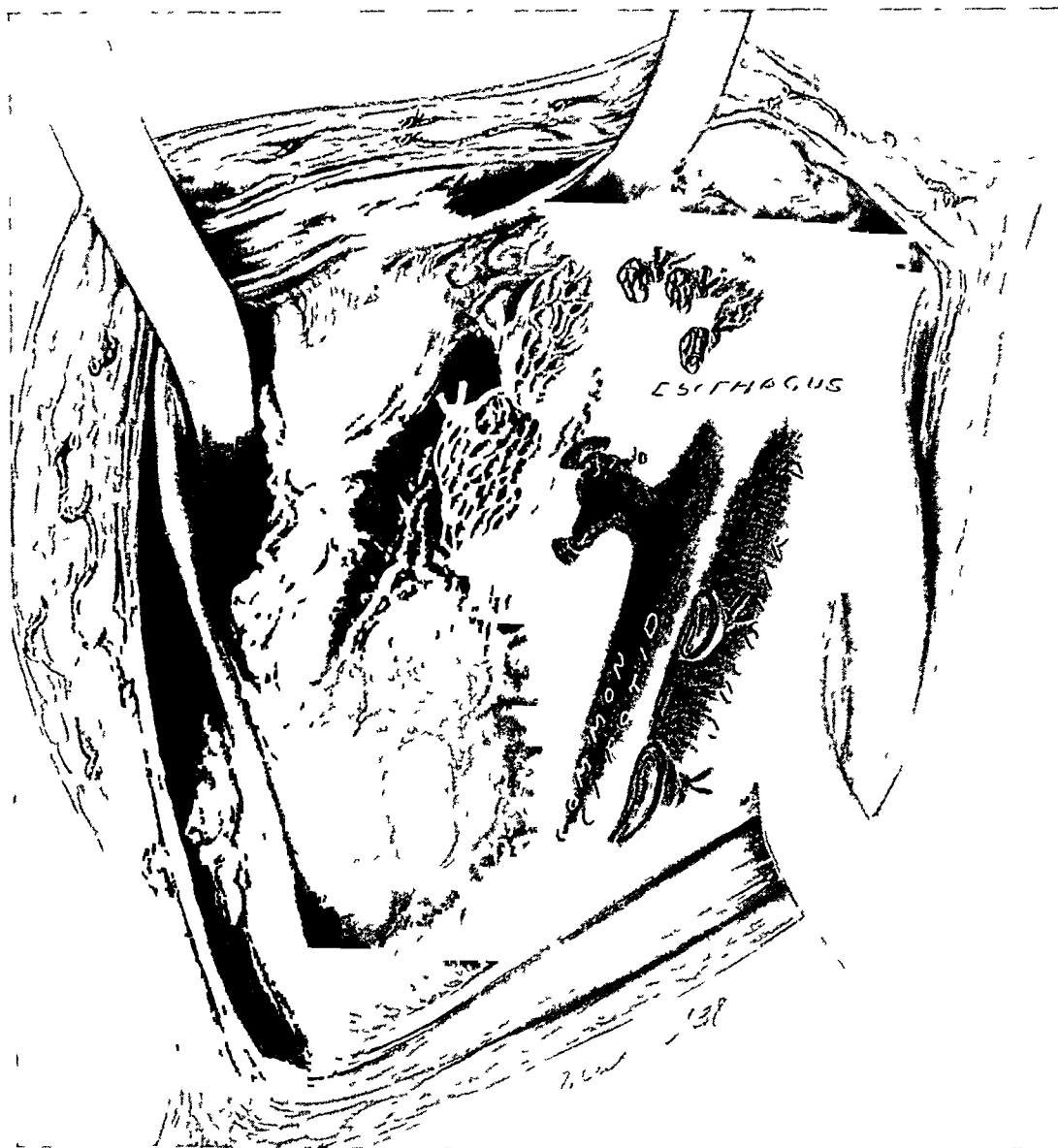


FIG 36—Case 30. Operation as completed. Esophagus is definitely involved. Lesion extends behind trachea to the right side of neck. Faint bruit still audible through a sterile stethoscope.

Operation—June 19, 1934. The incision extended from 4 cm below the internal condyle of the humerus well into the palm of the hand at the base of the fingers. The operation was performed without a tourniquet, and with the arm elevated far above the level of the heart. The angiomatous condition involved the surfaces of practically all the muscles, the nerves and the space between the flexor profundus muscle and the interosseus membrane. The blood encountered, though it was not excessive, was definitely arterial. Due to the greatly elevated position of the arm, we were able to shave off from the muscles and the nerves the greater part of this lesion without necessitating the

tying of many blood vessels. The belly of the flexor sublimis digitorum to the index finger was so involved that it was thought best to excise it. The tendon of this muscle was later sutured to the tendon of the flexor sublimis digitorum of the third finger. The



FIG 37—Case 16 Photograph of circoid aneurysm of right arm and hand before operation

ligatures used were fine, black silk, the skin incision was closed with interrupted, fine, black silk sutures. The arm was placed in a plaster encasement and suspended as far as possible above the patient by means of a Balkan frame. Although it was impossible

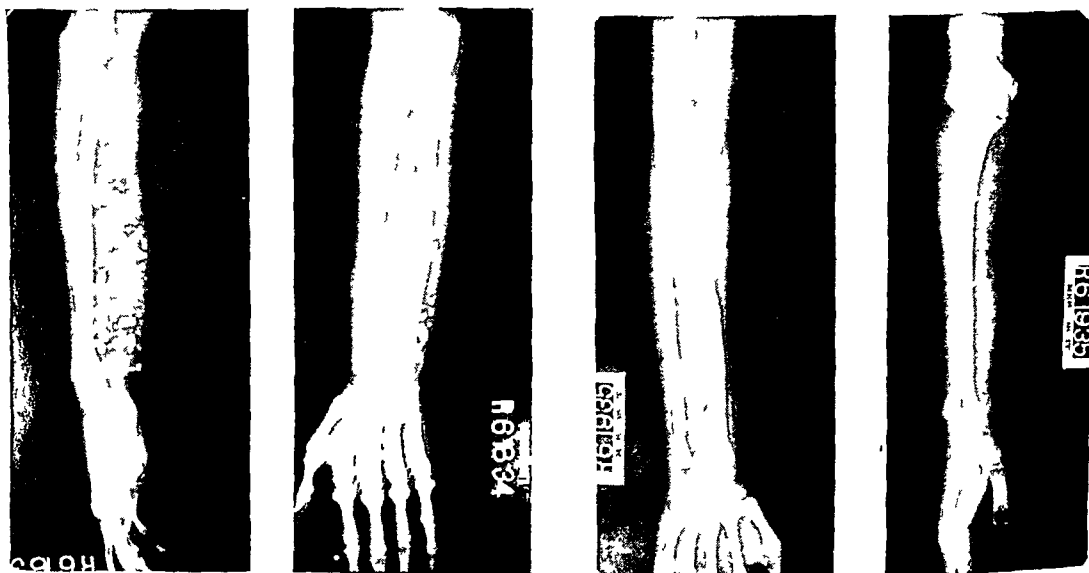


FIG 38—Case 16 Roentgenograms of right arm before and after operation

to remove all of this growth, it was felt that considerable thrombosis would occur in the remaining portion.

Subsequent Course—The patient has been observed regularly since the operation, the



FIG 39—Case 16 Photographs one year after operation



FIG 40—Case 16 Photographs three years after operation Very slight recurrence of cirroid aneurysm
Function of arm and hand perfect

last time being January, 1938, at which time there was practically no disability. The index finger apparently functioned quite normally (Figs 39 and 40). There was a little swelling above the wrist and in the palm but this had not increased materially during the past year. It was noted, in June, 1936, that the muscular development of the arm had practically returned to normal.

Experimental Studies—In connection with the study of our clinical cases there have naturally arisen many questions which we wished to study in the

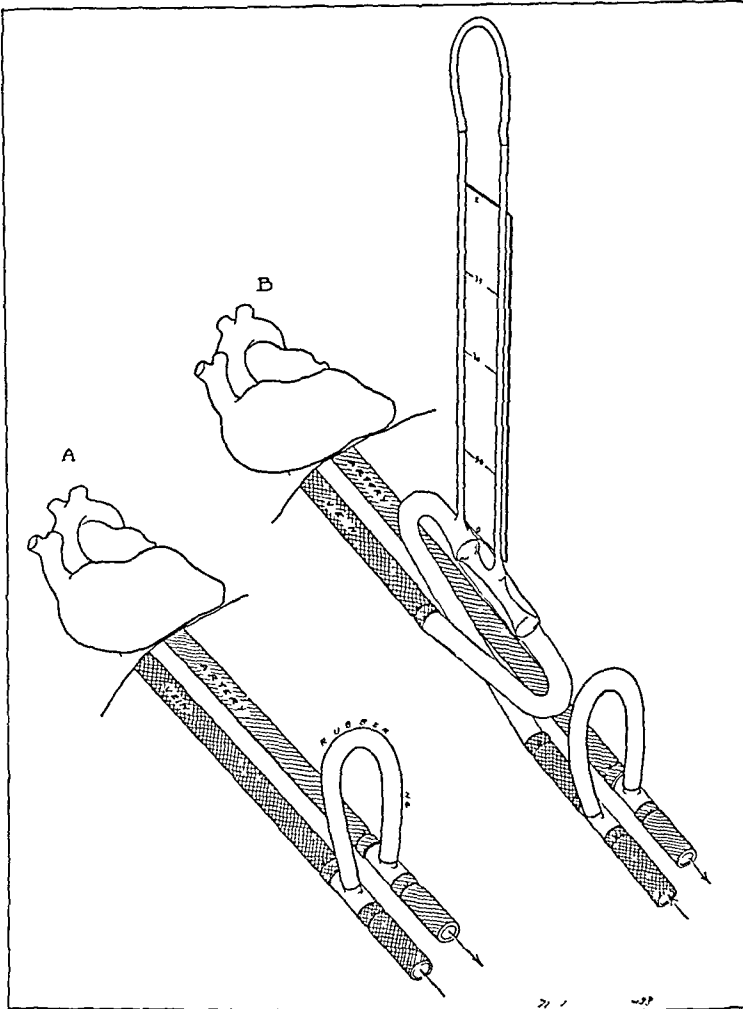


FIG 41—(A) Method of establishing an easily controllable fistula between the aorta and vena cava, used in some of our acute experiments. With the rubber tubing the fistula can be closed or opened as desired. Also, all the blood from the aorta can be easily diverted back into the heart. (B) Same as A, with a Venturi meter in the vena cava, to measure the volume of blood flow.

Laboratory of Experimental Surgery. We shall here refer only to experimental observations which we believe may shed some light upon our clinical studies or the previous observations of others who have interested themselves in the subject of abnormal arteriovenous communications.

The experiments have been both acute and chronic. In the acute, or non-survival experiments, communications were established between the abdominal aorta and vena cava (Fig 41 A) in four heparinized dogs. In two of these animals, in addition to the abnormal arteriovenous communication, a Venturi meter (Fig 41 B) was inserted into the vein between the site of the fistula

and the heart This instrument, based upon well known laws of physics, measures the velocity of flow regardless of the pressure of the fluid From this data the volume flow may be determined³ In five experiments direct

20	8/27/35 C G H No 445	December 1, 1935 Patient working steadily but still some exophthalmos, and a faint bruit and slight diplopia Unable to trace patient since
21*	5/13/36 C G H No 562	This patient was not operated upon because of extensive pulmonary tuberculosis and syphilis The thrill and bruit became gradually less and finally all signs of the fistula disappeared Months after the accident, the paralysis was mainly of the ulnar nerve and this, too, improved rapidly after the closure of the fistula
22	9/16/36 C G H No 6178	It was impossible to perform a complete excision because of the infiltration in the bellies of the muscles and between the bones Following the operation some sclerosing injections were introduced into the large vessels of the dorsum of the hand and fingers There is marked improvement in the function of the hand Operation was performed with arm suspended straight in the air to lessen hemorrhage
23*	10/29/36 C G H No 6374	Patient died February 11 1937, from extensive bilateral tuberculosis of the lungs Specimen of vessels obtained Fistula closed
24*	4/16/37 C G H No 73329	Patient was orthopedic, numerous taps for hydrothorax, operation under local anesthesia, with the patient in Fowler's position, marked improvement on table when fistula was closed Has resumed work
25*	4/16/37 C G H No 73338	This patient had multiple communications between external jugular vein and branches of external carotid artery, mainly a large occipital artery
26	6/13/37 C G H No 25847	This patient was discharged to wait for collateral circulation before operating Unable to get in touch with him since then
27*	9/10/37 Christ Hospital No 11254	Heart decreased in size Blood and plasma volumes decreased approximately 25% after operation, circulation time became 4 to 5 seconds longer All complaints disappeared
28*	10/22/37 C G H No 81335	Patient was operated upon early because of the rapid progressive paralysis of the radial nerve, and the fear of rupture of the aneurysm Two veins as well as the artery were involved No circulatory disturbance after operation Paralysis of the nerve has disappeared (February 15, 1938)
29*	10/10/37 2/10/38 C G H No 80815	Slight cardiac damage Pulse in foot reappeared after excision of the aneurysm Blood volume not increased during the four months Branham's bradycardic phenomenon present, also, elevation of blood pressure on closure of the fistula
30*	2/9/38 C G H No 88134	Definite cardiac enlargement with murmur Communications were definitely demonstrated at time of operation Immediately after ligating the right external carotid artery (4/26/38) bruit markedly decreased, but still faintly audible

* Reported in

last time being January, 1938, at which time there was practically no disability. The index finger apparently functioned quite normally (Figs 39 and 40). There was a little swelling above the wrist and in the palm but this had not increased materially during

meter (Fig 41 B) was inserted into the vein between . . .

and the heart. This instrument, based upon well known laws of physics, measures the velocity of flow regardless of the pressure of the fluid. From this data the volume flow may be determined.³ In five experiments direct anastomoses were made between the abdominal aorta and vena cava. In our chronic experiments we have in the laboratory two dogs with large fistulae between the iliac artery and vein.

A summary of our findings in the acute or sacrifice experiments is presented in Chart 1. In three dogs the cardiac output, as determined by the direct Fick method, increased an average of 1.75 liters when the aortic-venal caval fistula was open. This was an increase of over 100 per cent. Altogether, six determinations were made upon these three dogs.

The circulation time was determined by the sodium cyanide method.⁴ When this drug was injected into the vena cava about one inch above the fistula, the circulation was *reduced* an average of 4.5 seconds, whereas, the circulation time in the femoral vein, below the fistula, *increased* by an average of 3.9 seconds. Altogether 13 determinations were made upon the two dogs.

The venous pressures measured in the femoral vein increased on an average of 16.8 cm of water, whereas, two inches above the fistula (*i.e.*, between fistula and heart), there was an average increase of only 3.8 cm of water. These figures were based upon eight determinations made upon the four dogs. Inasmuch as the rise of venous pressures above the fistula was so slight and quite contradictory to the findings of Holman⁵ and Ney,⁶ we wondered if the venous pressure changes might be seriously altered by the rubber tube which formed the fistula between the aorta and vena cava. Consequently, some direct anastomoses were made just above the bifurcation of the aorta, and venous pressures, determined through the renal vein, were essentially the same as when the rubber tube was used for the connection of the aorta and vena cava. In no instance were we able to obtain the high venous pressures, well above the fistula, as were reported by Holman and Ney. The

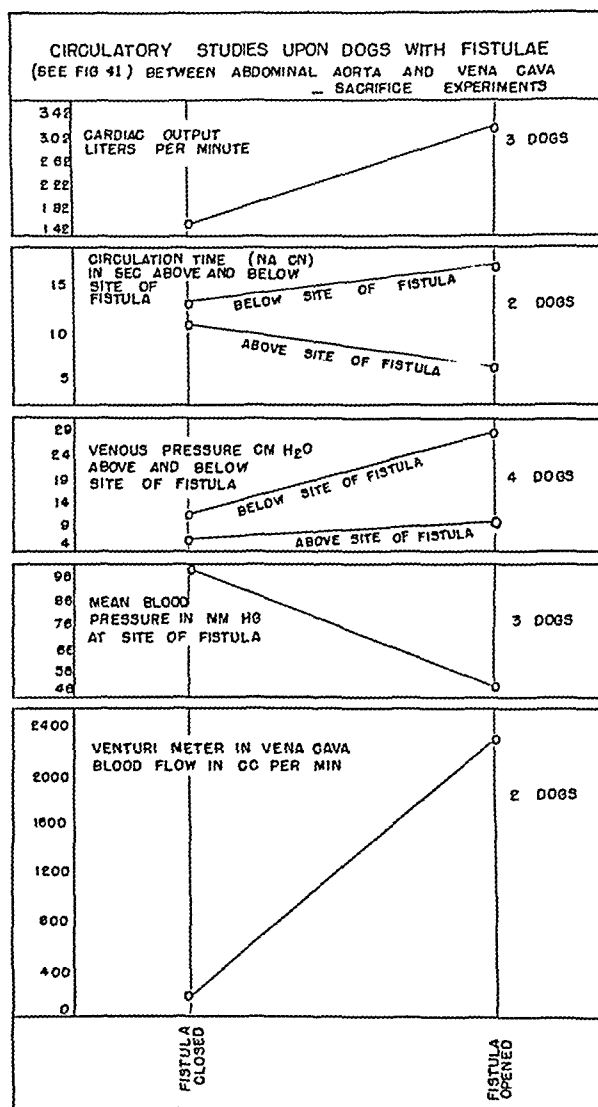


CHART 1

tremendous increase in cardiac output may, we think, explain the low venous pressures we obtained. Below, or distal to the fistulae, our observations were similar to those of other observers.

The mean blood pressure in the artery at the site of the fistula dropped an average of 49.6 Mm. Hg. in 12 determinations upon three dogs.

In two dogs, 13 measurements were made with the Venturi meter (Chart 1) of the amount of blood flow in the vena cava, both when the fistula was closed and open. There was an average increase of 2,090 cc. per minute through the vena cava above the fistula, when it was open. So far as we know, this is the first time the actual amount of blood flowing through this segment of vein has been measured in both the presence and absence of a fistula between the aorta and vena cava lower down. The amount of the increase of blood flow, when the fistula was open, was astounding to us, and when the aorta just distal to the fistula was temporarily occluded, the increase of the blood flow in the vena cava was far greater still.

There were a few other observations, perhaps worthy of note, in addition to those which are charted. For instance, whenever the fistula was opened, there was uniformly an increase of about 20 per cent in the heart rate. In one animal when all the aortic blood was diverted back through the vena cava into the heart, a systolic cardiac murmur developed in about five to seven minutes, and this disappeared in a similar period when the fistula was again closed. If, under this circumstance, the fistula was not closed shortly after the development of the murmur, cardiac failure seemed imminent.

By means of teleoroentgenograms we could not demonstrate any decrease in the size of the heart when the fistula was open. On the contrary, when the hearts of these dogs were exposed, all observers agreed that the heart, especially the right ventricle, became larger within less than a minute after opening the fistula. This increase was, also, roughly confirmed by measurement with calipers. Nor in our survival experiments have we been able to demonstrate any temporary decrease in the size of the heart after making the fistulae. These observations do not coincide with those of Holman, who noted decreases in the size of the heart for several hours or days after producing large arteriovenous fistulae in dogs, but do coincide with those of Lewis⁷ who, after the lapse of a few beats, noted a steady increase in the size of the heart.

In the two chronic or survival experiments with large iliac arteriovenous fistulae, the usual changes have been noted—cardiac enlargement, Branham's bradycardic phenomenon, rise of blood pressure on closure of the fistula, *etc.* The venous pressures in the limb below or distal to the fistula have remained constantly elevated, whereas these pressures in the neck have not increased since the fistulae were made. Also, in this connection, it should be noted that not as yet (Exper. 1, 18 weeks' duration, Exper. 2, nine weeks' duration) have there developed any evidences of cardiac decompensation.

Up to this point the blood volumes, as determined by brilliant vital red dye, have not increased. The blood volume made before operation in Dog

No 1 was 1,955 cc , since operation, 1,781 cc , before operation in Dog No 2, 1,815 cc , since operation, 1,745 cc

Discussion of Clinical and Experimental Observations—The 30 cases may be classified as follows (1) *Arteriovenous aneurysms*, 21 cases Of these there were six femorals, four popliteals, three brachials, two internal carotids, two intracranials (pulsating exophthalmos), one axillary, one subclavian, one ophthalmic, and one intercostal (2) *There were nine cirroid aneurysms* which may be classified as to location as follows Neck, three, leg and foot, three, arm and hand, three One of these cases (No 30) had four spontaneous cirroid aneurysms but is classified as one neck case because of the situation of the major lesion In this case there were two other cirroids in the left forearm and one on the dorsum of the left foot

Six of these cases were never operated upon In the 24 cases which were operated upon there was a total of 39 operations In the entire group there was not a death which could be attributed to the aneurysm or the operative procedures It is known that Case 2 died from pulmonary tuberculosis two and one-half years after the operation, and Case 22, from the same cause, three and one-half years later In both instances the aneurysms were cured All of the arteriovenous aneurysms operated upon, except one case (No 20) of pulsating exophthalmos, were cured, and two cases (Nos 10 and 20) healed spontaneously without operation Of the nine cases of cirroid aneurysm there appear to be only three complete cures (Nos 9, 16 and 25), and one of these cures was brought about by amputation All of the others have been benefited to varying degrees and none of them have lost an extremity

A study of all of these cases and the results of our experimental work lead us to make some comments upon the effects, and the treatment, of arteriovenous and cirroid aneurysms In most instances this work confirms previous observations reported by Halsted,⁹ Matas,¹⁰ Holman,⁵ Lewis,⁷ Reid¹ and many others In view of the recent complete bibliographies given by Holman and others, reference to the extensive literature on this subject will be made only when our conclusions and observations are at variance with those of other investigators

Damage to the Heart—The causal relationship between arteriovenous and cirroid aneurysms and cardiac damage has been definitely established since Reid first observed it experimentally, in 1918 Holman's splendid work in this connection no longer leaves room for doubt The main effects of the fistulae are cardiac enlargement, principally of the right ventricle, and eventual decompensation The degree of cardiac damage is directly dependent upon the vessels involved and the size of the fistula, the larger the vessels and the bigger the fistula, the greater is the damage to the heart In other words, the size of the spillway and the amount of arterial blood spilled directly over into the vein seem to be the major determining factors The effects upon the heart of the altered blood pressures and the proximal dilatation of the artery have not been definitely determined The heart, in the chronic cases, is rarely affected seriously unless the artery between the fistula and heart is definitely

dilated, and one cannot escape the feeling that whatever is responsible for this change in the artery may also be effective upon the heart

In this series of cases there were eight arteriovenous aneurysms which had caused definite cardiac damage (Nos 3, 6, 8, 15, 21, 24, 27 and 29). In two cases (Nos 6 and 24) there was severe cardiac decompensation. Of the cases of cirroid aneurysms two (Nos 17 and 30) showed evidences of some cardiac damage. In every instance where the heart was demonstrably affected, closure or excision of the fistula was followed by improvement in the condition of the heart. In Case 24 (Fig 7) the reduction in the size and the improvement in the function of the heart were quite astounding.

The Effect of Fistulae Upon Involved Vessels—The "venafication" of the artery between the fistula and heart is exemplified by the thinning of its wall, tortuosity and marked dilatation. Indeed, in some of these proximal vessels there have been reported true arterial aneurysms. In these vessels there was a great fall in systolic blood pressure. This reduction of strain or work upon the vessel wall probably accounts for its atrophy, which is evident in microscopic sections. Perhaps the blood pressure alterations reduce the nourishment to the vessel wall through the vasa vasorum. In any event, the atrophy of the proximal artery appears to confirm Thoma's old theory that a normal pulse pressure is essential to the integrity of an artery.

The "arterialization" or hypertrophy of the involved vein is logically explained by its increased work and adaptation to heightened pressures. That the vein between the fistula and heart carries a tremendous increase in volume of blood is shown by our studies with the Venturi meter upon dogs, where the average increase in volume of blood flowing through the vena cava between the aortic-vena caval fistula and heart was 2,090 cc of blood (Chart 1). From inspection it appears that very little true venous blood can find its way back to the heart through this segment of vein when the fistula is open, the force of the arterial spillway appears to let very little of the venous blood pass by the fistula.

In the artery and vein opposite the fistula extensive calcification was noted in the walls of the vessels. The explanation for this is not obvious to us.

In this series of cases there were 11 (Nos 3, 6, 8, 13, 15, 17, 23, 24, 25, 27 and 29) which showed definite enlargement, and thinning of the wall of the proximal artery. In Case 24, where the proximal artery was so very large and thin-walled, there appeared to be imminent danger of rupture of the artery proximal to its ligation. In many cases the wall of the involved vein was definitely hypertrophied.

The Circulation Time—Studies of the circulation time, employing the sodium cyanide method, were made upon six patients (Nos 15, 21, 25, 27, 28 and 29) and on all of our experimental dogs (Chart 1). A very striking finding, which was not unexpected, was an acceleration of the rate when the drug was injected into the vein between fistula and heart, and a very definite retardation when it was injected on the opposite or distal side of the fistula. When the drug was injected into veins in parts of the body far removed from

or not directly affected by the fistula, there was no positive evidence that the circulation time was definitely affected by the fistula, in a few cases (Nos 27, 28 and 29) it was about three seconds faster when the fistulae were present than it was after their extirpation, while in Case 25 it was four seconds slower than it was after operation. However, no circulation times were made upon patients with cardiac decompensation resulting from arteriovenous aneurysms. In the one case (No 24) the patient was so sick we were loath to use the test. Similar studies have been reported by Porter¹⁵

Blood Volume—Blood volume determinations were made upon Cases 25, 27 and 29, and in the case of our two survival experiments upon dogs. In Case 25 there was a drop of 1,000 cc 11 days after the operation, but nine months after the operation it was practically the same as before operation. In Case 27 there was a drop of 600 cc in blood volume 13 days after the operation and there have been no determinations since then. In Case 29 there was an increase of 400 cc three weeks after the operation. In all of the observations upon dogs, even though the heart has definitely enlarged, there has been no increase in blood volume, in fact, there has been a decrease of 174 cc in Dog No 1 and of 70 cc in Dog No 2. In none of the patients upon whom these studies were made was there congestive heart failure.

Our studies, thus far, fail to confirm the observations of Holman⁵ and others, who have reported a large increase in blood volume in cases of arteriovenous aneurysms. That an increase would occur in cases of heart failure due to arteriovenous fistulae should be expected, inasmuch as Gibson and Evans¹¹ have shown it to be the case in all instances of congestive heart failure regardless of the cause. But the necessity for its occurrence in cases of arteriovenous fistulae, without heart failure, seems to us questionable. The increase of pulse rate and the enormous increase of cardiac output are quite sufficient to explain the cardiac damage, without the necessity of postulating an increased blood volume. Besides, we doubt the accuracy of the dye method of determining blood volume in these cases, inasmuch as the normal dissemination or dilution of the dye must be markedly altered by the presence of a large arteriovenous fistula.

Brianham's Bradycardic Phenomenon—The slowing of the pulse rate, when the fistula was closed, was noted in ten cases (Nos 6, 8, 12, 13, 15, 18, 24, 27, 29 and 30) and in all of our experimental animals. The extent of this slowing of pulse rate varied greatly and seemed to be directly related to the seriousness of the cardiac damage and the size of the fistulae. For instance, in Case 24, where there was very serious cardiac failure (Fig 7), the pulse rate dropped from 80 before operation down to 40 three hours after it. The cause of this phenomenon, as so well discussed by Holman, is undoubtedly related to the sudden rise in blood pressure which either reflexly or directly stimulates the cardio-inhibitory center of the brain, or possibly has a direct effect upon the myocardium.

Venous Blood Pressures—Observations upon the venous pressures were made in nine of our cases (Nos 8, 15, 17, 21, 24, 25, 27, 28 and 29). When

these pressures were taken in parts of the body far away from the direct or local effects of the fistula, there was no noticeable effect upon the general venous pressures as long as there was no cardiac decompensation. For instance, when observations were made in the arm, in the case of a femoral arteriovenous aneurysm, there was no appreciable change in the venous pressures on closing the fistula or following its operative cure. However, in Case 24 with a femoral arteriovenous aneurysm, when there was severe cardiac decompensation, the venous pressure in the right arm was 25 cm of water and was unaffected by temporary closure of the fistula, after operation and when the heart was completely compensated, it dropped to 5 cc of water, or normal. Thus it would seem a logical conclusion from our studies that the general venous pressures are unaffected by arteriovenous aneurysms unless there occur some evidences of cardiac decompensation, when the changes in venous pressures are similar to those which occur in cases of cardiac decompensation from any other cause. We would feel that a marked rise in the general venous pressures might be considered evidence of impending myocardial failure even though this was not obvious clinically.

Our studies of venous pressures in an extremity above and below the site of a fistula do, perhaps, deserve some special comment in view of the reports by Holman and Ney that such pressures are markedly increased in the vein proximal to the fistula. In Case 29, a right popliteal arteriovenous aneurysm, the venous pressure in the femoral vein, as measured by the direct method, was $5\frac{3}{4}$ cm of water with the fistula open, and $4\frac{1}{2}$ cm when it was closed. At the same time the venous pressure in both antecubital veins was 10 cm of water. Three weeks after the operation the venous pressures in these same three vessels were 7.75 cm of water. In several cases the venous pressures distal to the site of fistula were markedly elevated as long as the fistula was open and promptly dropped to the general normal level when the fistula was closed or cured. These clinical observations coincide exactly with our experimental studies (Chart 1). This very slight rise of venous pressure between the fistula and heart was an unexpected finding. Perhaps the enormous increase in cardiac output (Chart 1) relieves the pressure within the vein as long as the heart is compensating for the increase in amount of blood it has to handle.

Blood Pressure Changes—A rise in both systolic and diastolic pressures following closure of arteriovenous fistulae was noted in 13 cases (Nos 6, 8, 12, 15, 17, 18, 23, 24, 25, 27, 28, 29 and 30). In some cases this rise was quite striking, as in Case 24, where it rose from 140/40 to 190/90 almost immediately on temporarily closing the fistula. Following operation this increase of the arterial pressures gradually falls until at the end of ten to 14 days it becomes stabilized or normal. The permanent rise of the diastolic pressure is more striking than the alteration of the systolic, which may ultimately return to the preoperative level.

In three cases with fistulae in the neck (Nos 23, 25 and 30) there were very pronounced elevations of the arterial pressures during dissections of the

carotid sinus, even before anything had been done to the arteriovenous fistula. In Case 23, during manipulation of the carotid sinus the pressure rose from 120/100 to 170/110. In no case was there a permanent rise in blood pressure, in two cases the pressures returned, after two weeks, to levels slightly below the preoperative values.

Collateral Circulation—There were six cases (Nos 6, 8, 13, 15, 24 and 29) in which our observations confirmed other clinical and experimental evidences that around an arteriovenous fistula there occurs a very extensive collateral circulation. In several cases peripheral pulses which were not palpable as long as the fistula was open could be made to appear by simple pressure closure of the fistula, and after operation they appeared and remained good. Curiously enough, the pulse may appear, for the first two or three postoperative days, to be stronger than in the opposite extremity. After this there is a gradual and definite decrease in the volume of these pulses for a period of about ten days.

It is this overabundant collateral circulation which makes the occurrence of gangrene after excision of chronic arteriovenous fistulae practically unknown.

Impairment of Peripheral Circulation—The circulation, considerably distal to the fistula, may be markedly impaired as evidenced by absent pulses, coldness of the part, cyanosis and occasional chronic ulcers which will not heal. This impairment, in varying degrees, was noted in five cases (Nos 6, 8, 12, 13 and 15). In Case 15, a popliteal arteriovenous aneurysm, there had been a chronic ulcer of the shin for a long time and occasionally there had occurred serious bleeding from it.

Effect on the Growth of Extremities—In the region of arteriovenous fistula, especially in those cases of cirroid aneurysms where there are multiple fistulae, there appears to be increased circulation. In addition to an elevation of surface temperature and the known elaborate collateral circulation, another evidence is the occasional increase in the length of an extremity when the fistulae are present before the time of the ossification of the epiphyses. This was noted in five of our cases (Nos 5, 9, 13, 17 and 22). Naturally the most striking increases in the length and size of extremities are to be noted in the cases of cirroid aneurysms which are usually congenital, contain numerous arteriovenous fistulae and extend over large areas. This was especially observed in Case 9, which was reported in detail in the J A M A, 191, 1391-1393, October 28, 1933.

Associated Nerve Paralysis—In four cases (Nos 12, 13, 18 and 28) there were nerve paralyses associated with the arteriovenous condition. In Case 12, this was produced by the gunshot wound and was not repaired at the time of curing the fistula. In the other three cases the paralysis seemed to be secondary to the arteriovenous aneurysms. In Case 13, we could find no injury to the peroneal nerve at the time of the operation except that it was infiltrated and distended by pulsating varicose veins (Fig 1). That this was the probable cause of its paralysis seems to be justified by the fact that, after curing

the aneurysm, the paralysis disappeared. In Case 18, the pulsating axillary veins, together with a large amount of scar tissue, appeared to be the cause of the paralysis. After excising the aneurysm and removing most of the scar tissue, the paralysis of the arm disappeared. In Case 28, the paralysis of the median nerve was clearly due to pressure of the pulsating, false aneurysmal sac in which the arteries and veins communicated. The return of function in this nerve was very prompt after excision of the aneurysm.

Double Arteriovenous Fistula—Occasionally the object which produces an arteriovenous aneurysm will penetrate two veins and the artery and establish a double fistula. This occurred in Cases 18 and 28. In Case 18, the surgeon who first operated cured only one of the fistulae, and it was necessary for us to operate, six months later, in order to cure the other (Figs 8, 9, 10 and 11). In the second case the condition was recognized at the first operation and both veins and the artery were excised (Figs 24, 25 and 26).

Arteriovenous Aneurysm Caused by Thoracentesis—This occurred in Case 10. After about five years the characteristic bruit and thrill reached their maximum intensity, subsequent to which the signs of the aneurysm began to subside, and at the end of 13 years from the time of the injury, there were no signs of a fistula, only a faint systolic bruit indicating a slight coarctation of the intercostal artery. There never developed a pulsating, angiomatous condition of the chest wall. Roentgenologic examinations of the thorax were always normal.

Intraocular Arteriovenous Aneurysms—There were two cases (Nos 2 and 20) of pulsating exophthalmos, and one instance (No 4) of a fistula between the ophthalmic vessels behind the eyeball. In Case 2 it was necessary, because of hemiplegia, to remove the aluminum band from the carotid artery eight hours after the operation. The hemiplegia promptly disappeared. Fourteen days later the band was reapplied, followed by a partial hemiplegia which entirely cleared up, except for a slight spasticity of the right arm. The aneurysm was cured. In Case 20, the external carotid artery was ligated, and the common carotid occluded by a metallic band. There were no cerebral symptoms, but the aneurysm was not completely cured at the last follow-up examination. In one case, the record of which cannot be found, the operative procedure was to divide the supra-orbital vein and to scarify the intima of the proximal part in order to enhance the chances of a propagating thrombosis which might occlude the fistula. Nothing was done to the vessels of the neck. Following this procedure, and with bed rest in a high Fowler's position and limitation of the fluid intake, there was a marked improvement, but not a complete cure.

In Case 4, arteriovenous fistula between the ophthalmic vessels, the following procedure was undertaken: (1) Ligation of the external carotid artery with braided silk. (2) Occlusion of the common carotid by an aluminum band. (3) Excision of veins from the upper eyelid and inner side of nose. Six months after this operation, a harsh bruit at the site of the band indicated that a lumen was being established in the common carotid artery. At the last

examination, April 13, 1938, the patient was entirely well. The eye was normal. At the site of the band, a faint systolic bruit indicated a good lumen beneath it. There was a strong temporal pulse which disappeared on occluding the common carotid artery. No dilatation of this artery was noted, either proximal or distal to the band, it appeared to be normal in size.

Spontaneous Healing—In this series of cases there were two arteriovenous aneurysms which healed spontaneously. The fistula in Case 10 was between the intercostal vessels, in Case 21, between the subclavian vessels. A similar case was reported in Reid's previous series and recently Bird¹² has reported other instances. It is not an unusual occurrence in experimental fistulae between the smaller vessels.

In view of these experiences it is probably wise to use every effort to promote spontaneous healing before resorting to surgery. A long period of rest in bed, with elevation of the affected part and the limitation of fluid intake, possibly bleeding, soon after the accident, might result in more spontaneous cures. Certainly the long period of bed rest for tuberculosis was a big factor in the spontaneous healing in Case 21.

Time to Operate—Unless immediate or early operations are required because of hemorrhage, dangerous hematoma or infection, or rapid cardiac damage, we believe it wise to postpone operating for three to six months after the occurrence of the fistula. During this period hemorrhage becomes absorbed, tissues restored to normal, danger of infection lessened, and collateral circulation becomes so extensive that there need be no hesitancy in sacrificing the involved vessels at the time of operation. Mason¹³ and Stone¹⁴ have reported two cases in which the cardiac damage developed so rapidly that they could not wait for the development of a collateral circulation. This did not occur in any of the cases reported in this paper. However, it was necessary to operate early in Case 1, because of infection and secondary hemorrhage, and in Case 28, because of impending hemorrhage and rapidly progressive median nerve paralysis. A rapidly rising general venous pressure should probably be regarded as an indication for early operation, even though the heart may not appear, clinically, to be badly affected.

During the period of time that operation is being delayed, it is our feeling that more effort should be made to improve the chances of spontaneous healing than has been made in the past. Keeping the patient in the hospital during this time not only allows the adoption of measures to promote spontaneous healing, but also is the surest way of remaining in touch with charity patients. In our series of cases we were never able to trace three patients who promised to come back for later operations (Nos. 3, 7 and 26).

Standard Curative, Operative Procedures—The essential thing in the operative cure of arteriovenous and cirroid aneurysms is to eliminate all possibilities of any blood ever again passing through the fistulae. The procedures which have been used and which accomplish this end are

(1) *Closure of the Fistula, with Restoration of the Vein and Artery*—This procedure would appear, at first thought, to be ideal and physiologic

However, in many cases this has been followed by serious pulmonary complications, due to embolisms of air, and blood clots from thrombosis at the site of the operation. Besides, the enormous venous dilatations in old cases make it unnecessary. The ligation of the involved veins probably results in a better balance between the arterial and venous beds, even though the artery is restored. This procedure was not carried out in any of our cases.

(2) *Suture of Fistula with Restoration of Artery and Ligation of the Vein*—When the arterial wall is not atrophied and no danger is anticipated from a sudden restoration of normal blood pressure, there is no objection to this procedure. It is particularly desirable where operations are performed early, as is frequently done in Europe, and before there has been time for the development of an adequate collateral circulation. In the late cases where severe changes have occurred in the proximal artery and there is abundant collateral circulation, we do not believe in attempting to restore the artery. It is not necessary, and occasionally there develops a true arterial aneurysm after closure of the fistula. This happened in a case reported previously by Reid.¹ This procedure was not done in any of the cases reported in this series. When one elects this operative procedure, a part of the vein can often be used to advantage in closing the defect in the artery.

(3) *Quadruple Ligation of the Artery and Vein*—This procedure is certain of succeeding only where all the intervening branches are ligated, otherwise, the chances of the return of the aneurysm to its previous state are excellent. In addition, this procedure carries the additional dangers of ligation in continuity as compared with those of division of the artery.

(4) *Ligation of the Canal of Communication*—This procedure is probably dangerous and, besides, is rarely possible technically. It was done in one of Reid's early cases where the fistula was only six months old, and the canal of communication small and easily identifiable.

(5) *Extirpation of Both Vein and Artery at the Site of Fistula, with Quadruple Ligation of the Vessels*—This was done, whenever possible, in all the cases of this series. There must necessarily be exceptions to this procedure such as in the cases of intracranial arteriovenous aneurysms, certain extensive cirsoid aneurysms and, occasionally, under other circumstances which will be discussed later. Complete extirpation certainly obliterates the fistula and, in Reid's cases, has given most satisfactory results. Procedures which require the use of a tourniquet have, when possible, been avoided. For this reason we have had little experience with the Matas intrasacular restorative and obliterative procedures. In a few cases where we have elected this method of operating, the control of hemorrhage, after removal of the tourniquet, has been more troublesome than when a slow dissection was made without a tourniquet. This was especially true in Case 12 of our series.

(6) *Ligation and Division of the Involved Vessels and Transfusion Occlusion of the Fistula*—This is a procedure which has been employed in two cases (Nos. 13 and 24, Figs. 1, 2, 3, 4 and 5), and seems to us to be an effective method of assuring the closure of the fistula when the hazards of

total ablation appear to be too great. There is no danger of hemorrhage from puncturing the vein with double braided silk after the ligations of the artery and distal vein.

(7) *Closure of the Fistula by Means of Dividing and Twisting the Vein* — This is probably a new procedure and was effectively employed in Cases 23 and 25 (Figs 12, 13, 14, 19, 20, 21 and 22). In these two cases it was impossible to expose the vessels distal to the point of the fistulae. In one case (Case 23) it was obvious that the patient would not tolerate a proximal ligation of the artery in addition to the twisting of the vein. Yet the autopsy, a year or more later, showed that the fistula was completely healed without any disturbance in the lumen of the artery. This technic of operating appears to us to have a definite application in some of those cases where it is not possible to use any of the other standard, curative procedures which have been discussed. Since the idea of this operative procedure occurred to us, we have not had a case of pulsating exophthalmos in which we would like to divide and free and twist the proximal portion of the supra-orbital vein in addition to whatever else might be undertaken in the neck.

Palliative Operative Procedures — In old cases, when the heart is badly damaged, there may be some question as to whether the heart can stand the physiologic change incident to a sudden closure of the fistula. Both Matas and Holman have spoken of this and have advocated, and cite, the employment of such procedures as repeated temporary digital compressions of the fistula in order gradually to accustom the heart to a permanent closure of the fistula. In none of the cases in this series did it appear necessary to adopt these preoperative procedures, although in Case 24, there occurred a rather alarming bradycardia after the operation and, at operation, the proximal artery came near rupturing when it was ligated.

In one of Reid's cases, reported in 1925, Halsted ligated the proximal vein with great relief to the heart. When the measures advocated by Matas leave a real doubt as to whether the heart can stand a sudden extirpation of the fistula, it might be well to consider preliminary ligations of the proximal, or even the proximal and distal vein, before performing the operation which will permanently close the fistula.

Mistakes in Operative Procedures — In general, any procedures which do not actually close the fistula are undesirable and run serious risks of not only failing to cure the aneurysms, but of causing serious circulatory disturbances peripheral to the fistulae. An untold number of limbs have become gangrenous and have had to be amputated because of the *simple proximal ligation of the artery*. It is far more dangerous than the ligation of an artery for an arterial aneurysm, for the shunt or spillway remains and there is no longer enough arterial force to push the blood beyond it. Although all authors discussing this subject in recent years have severely criticized the proximal ligation of the artery for arteriovenous aneurysms, it is still unnecessarily done. In Case 13 (Fig 1), the patient was made an invalid for over a year and almost lost his leg following a proximal ligation of the artery.

In the preceding paragraph we have used the word "unnecessarily," for there are some abnormal arteriovenous communications for which it still seems necessary to take the risk of performing a proximal ligation of the artery. In the case of the extensive cirroid aneurysm, where a direct attack upon the numerous fistulae is impossible, there is apparently no risk in ligating almost as many proximal arteries and veins as one can find (Cases 5, 9 and 10). Again in cases of pulsating exophthalmos (Nos. 2 and 20), and in such a case as Case 4, it would appear better to take the chances of a proximal ligation than to carry out the direct attacks upon the fistulae. In addition to ligating the external carotid and occluding the common carotid with a removable metallic band, we shall in the future try dividing and twisting the supra-orbital vein as has already been suggested. The ligation of the jugular vein, as advocated by Holman, should probably also be done.

SUMMARY

(1) An analysis of 21 cases of arteriovenous and nine cases of cirroid aneurysms is presented, which is supplemented by observations upon experimentally produced arteriovenous aneurysms in dogs.

(2) Sixteen of the arteriovenous aneurysms were operated upon and all of them, except one case of pulsating exophthalmos, were cured. In two instances the aneurysms healed spontaneously without operation. Four patients failed to return for later operations and could never be traced. All of the nine cirroid aneurysms were operated upon, three were cured and the other six were more or less improved. There were no deaths in the entire series of 30 cases. There was a total of 39 operations upon the 24 patients who were subjected to surgical treatment.

(3) Clinical and experimental observations which may throw some light upon the physiologic and pathologic effects of arteriovenous fistulae are discussed in some detail. The principal effects noted and studied were: Ten instances of cardiac damage, 11 instances of thinning and dilatation of the proximal artery, circulation time upon six patients, blood volume upon three patients, ten instances of Bianhan's bradycardic phenomenon, 13 instances of blood pressure alterations, studies upon the venous blood pressures of nine patients, nine instances of markedly increased collateral circulation, five instances of impairment of the circulation peripheral to the fistula, five instances of an increase in the size and length of an extremity, four instances of associated nerve paralyses, two instances of double arteriovenous fistulae, and two instances of spontaneous healing of the aneurysm.

(4) In our limited clinical and experimental observations, we could not confirm Holman's findings of a marked increase of the total circulating blood.

(5) A Venturi meter was used in some of the experiments to measure the flow of blood in a segment of the vena cava. An easy method of making an arteriovenous fistula which can be alternately closed and opened is illustrated.

(6) The time to operate, and the standard curative operative procedures are discussed. Two new operative procedures are illustrated and described in the case reports.

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DISCUSSION—DR JAMES M MASON (Birmingham, Ala) stated that Though first described by William Hunter, in 1757, surgery had added but little to the treatment of arteriovenous aneurysms until the period of the World War Osler vigorously opposed operation, and the outstanding contributions of American surgeons up to this time were the recognition and description by Branham, in 1890, of the bradycardic phenomenon which now bears his name, and the report by Matas, in 1902, of the successful operation upon a subclavian arteriovenous aneurysm, the sixth operation which had ever been undertaken for the relief of fistulae involving these vessels

The number of cases resulting from war wounds was enormous, and became the subject of critical study, which led Gundeimann, Caro, Makins, Cazaman and others, between 1915 and 1917, to suspect, and finally to recognize, a definite relationship between arteriovenous communications and associated heart lesions In 1914, Reid began his experimental work on vascular surgery under the direction of Halsted and stated that "In the course of two or three years we were fully convinced that a fistula between the large vessels of the neck or legs may cause marked hypertrophy and dilatation of the heart, and, in some instances, cardiac decompensation and death"

The clinical and experimental studies which were undertaken to establish this relationship have been among the most extensive and interesting in the history of medicine. Not until they proved the suspected relationship to be an established fact was the seriousness of arteriovenous aneurysms fully realized. Halsted's death, in 1922, prevented him from taking an active part in the further development of this type of vascular surgery, but the work initiated by him, and continued by his coworkers, has aided immeasurably.

The "Indications for Operation," so clearly stated by Reid in former papers, and the operative procedures which he then advocated, have withstood the most critical tests and are restated in his present paper. To these operative procedures he has added two ingenious methods of closing fistulae difficult of access or too extensive for excision, namely, twisting of the vein and fixation at the site of the fistula, and occlusion of the fistula by transfixion sutures after ligation of the vein and ligation of the artery.

Two questions in regard to arteriovenous aneurysms interest me greatly (1) Why, in some instances, do cardiac symptoms appear early and progress rapidly, while in others their appearance is delayed and their progress more gradual? (2) What measures may we safely employ when decompensation makes early operation imperative?

In my series of traumatic fistulae are one chronic and four acute cases involving the subclavian vessels. The chronic case was seen three years after his injury. The heart was seriously damaged, but he was at work as a chauffeur and refused operation. He is still at work, nearly eight years after his injury. In one of the acute cases, cardiac decompensation had reached a grave stage at the end of 30 days, and operation was carried out on the seventy-seventh day. In another instance, decompensation resulted in death on the fourth day before any operative measures were undertaken. In two cases operated upon at the end of four months, neither patient showed any heart symptoms of moment.

In the cases of early decompensation, little gross change in the vessels adjacent to the fistula was noted at operation or autopsy. The proximal veins were unobstructed, and, in one instance, seemed rather dilated. The cases without decompensation showed very large varicosities at the site of the fistula and immediately distal to it. In one instance, thrombophlebitis had developed soon after the injury and extended well down the arm. This, however, had subsided and no thrombus was present at the time of operation.

In the experimental fistulae of Holman and Stultz, quoted by Tixier and Arnulf, some cases failed to develop cardiac lesions. They attributed this to thrombosis in the vein proximal to the fistula, which prevented the rapid return of blood to the heart. Reid, Stone, and Holman have made the clinical observation that cardiac symptoms were much improved by proximal ligation of the vein. Tixier and Arnulf, and also Matas, have commented favorably upon the possibility of temporarily relieving early acute decompensation by proximal ligation of the vein, to be followed later, of course, by curative operation upon the fistula itself. The thrombophlebitis which was present in one of my cases may have extended into the proximal vein. The striking similarity in the varices in the other patient suggests the possibility of an unrecognized thrombophlebitis in that case.

In cases under my care there have been two spontaneous recoveries, one in the femoral vessels at the groin and one in the posterior tibial vessels just above the ankle.

DR JOHNSON McGUIRE (closing) I think the questions which Doctor Mason has asked are particularly interesting, especially those relative to the

cause for cardiac decompensation in arteriovenous aneurysms and the decision as to the proper time to operate

In one of the patients Doctor Reid has described, digitalis failed to improve the patient's clinical condition. In this case, progressive increase in the level of the venous pressure occurred. Consequently, operation was decided upon as an emergency procedure. Immediate improvement occurred.

As to why the hearts of certain of these patients become seriously damaged and others do not, we have felt that the size of the fistula is an important factor. With large fistulae, the heart has to pump a large volume of blood and is relatively quickly exhausted by excessive work. Also the fundamental condition of the heart muscle may be of significance, as a patient with arteriosclerotic heart disease would develop failure more rapidly than would a normal individual with fistulae of equal size.

The work of the heart may roughly be calculated if one multiplies the blood pressure by the cardiac output. It is our feeling that constant work, day and night, increases the amount of blood that the heart has to handle, as shown by the measurements with the Venturi meter, and is the probable cause of cardiac failure.

The theory of Sir Thomas Lewis, that heart failure in arteriovenous fistulae is caused by inadequate coronary blood flow, due to the fact that the diastolic aortic pressure is lowered, has been recently challenged, since measurements of coronary blood flow in the presence of artificial arteriovenous aneurysms have failed to demonstrate a significant decline of blood flow in the coronary arteries.

SPONTANEOUS ARTERIOVENOUS FISTULA BETWEEN THE ABDOMINAL AORTA AND THE INFERIOR VENA CAVA

CASE REPORT

PRESENTED IN DISCUSSION OF THE PAPER BY DOCTORS REID AND MCGUIRE
ON ARTERIOVENOUS ANEURYSMS

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ABNORMAL arteriovenous communications are properly divided into two groups—the congenital and the acquired. The latter group is subdivided into those of traumatic origin, which represent, by far, the largest group of arteriovenous fistulae, and those of so-called spontaneous origin. The latter are the result of disease of the arterial wall, they are caused, in almost all instances, by syphilitic aneurysms that have perforated into contiguous veins. These lesions represent the rarest type of arteriovenous fistula. Although a few cases of spontaneous acquired lesions in the peripheral vessels are on record, it is probable that they have been confused at times with congenital fistulae. Most of the true spontaneous fistulae are complications of aortic aneurysm and occur within the thorax, where perforation may take place into the superior vena cava, the pulmonary vessels or the heart itself. Up until 1930, there had been recorded about 75 instances of spontaneous communication between the aorta and the superior vena cava,^{1 2 3 4 5} and a somewhat characteristic clinical picture has been described.

Spontaneous fistulae below the diaphragm are apparently very unusual. Matas,⁶ in 1909, stated that Boinet, in collecting 114 spontaneous arteriovenous fistulae, had found only 20 that involved the abdominal aorta and the inferior vena cava. Reid,⁷ in 1925, added no other references, and a complete search of titles, since 1925, revealed no further reports. It is possible, of course, that further examples may be hidden in the rich literature of arteriovenous fistulae, which has not been exhaustively searched. The relative rarity of the abdominal lesion as compared to the thoracic lesion is, of course, explained by the relative infrequency of abdominal aneurysm as compared to thoracic aneurysm.

The appended history of a case of spontaneous arteriovenous fistula connecting the abdominal aorta and the inferior vena cava is reported.

Case Report—University of Virginia Hospital No 114,836 J. A., colored, male, age 37, entered the hospital February 1, 1935. The patient had been married for 15 years, his wife had never been pregnant. The past history was unimportant, except for the occurrence of a chancre about ten or 12 years previously. At that time he had been treated with four injections in the arm. In childhood he had received severe barbed wire cuts over the left abdomen and chest.

He had been in good health until 18 months before entrance. At that time he began

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to have pain in the lower part of his back, with swelling of his legs. He was given magnesium sulphate for his edema and several injections in the arm. He improved somewhat until six months before entrance, when both the swelling and the pain became worse. Two months later, he noticed enlargement of the veins of his abdomen and chest, and, two weeks before entrance, a "knocking" over his right abdomen. There was no dyspnea, orthopnea, hemoptysis, or cough. There had been no disturbances in the neuromuscular mechanism, and there was no history of recent injury.

FIG 1

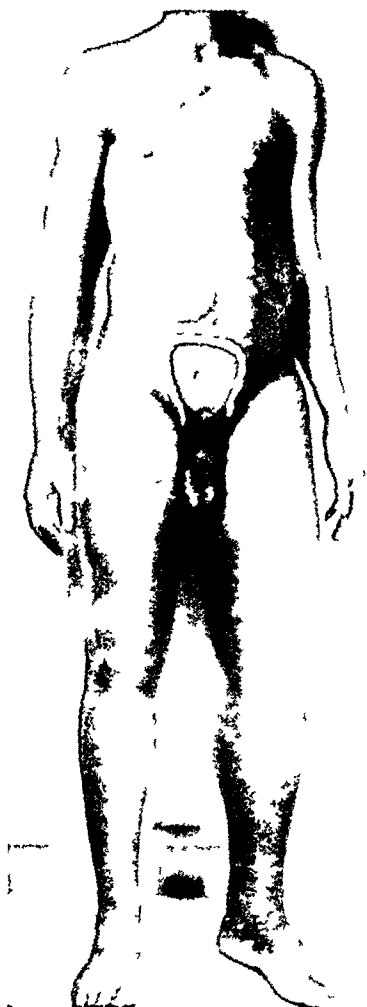


FIG 2



FIG 1—Photograph of the patient showing the swelling of the legs and scrotum, dermatitis of left shin, enlarged superficial veins, scars of barbed wire cuts on abdomen and chest, and the outline of the abdominal masses.

FIG 2—Photograph showing the enlarged left thoraco epigastric vein and scars of the barbed wire cuts.

Physical Examination revealed a rather undernourished Negro with marked swelling of the legs that hampered his walking (Fig 1). In the left upper abdomen, parallel to the costal margin, was a long keloid, representing the barbed wire cut of childhood. A similar scar crossed the right upper chest. The veins in the upper thighs, the epigastric veins and the anterior thoracic veins were markedly dilated and tortuous (Fig 2). The veins over the scrotum were enlarged and a marked degree of varicocele was present.

A diffuse apex impulse was seen and felt most prominently in the fifth interspace about 3 cm lateral to the midclavicular line. A loud systolic murmur was heard all over the precordium. No definite diastolic murmur was present, but the second sound was accentuated. The murmur was transmitted to the neck and axilla. The rhythm

was regular and the rate ranged between 80 and 90. The systolic blood pressure in the arms averaged 160 and the diastolic 70, the average pulse pressure, therefore, being about 90 Mm Hg.

Abdominal palpation revealed two masses. To the right and just above the umbilicus (Fig 1) there was felt a mass about 8 cm in diameter, spherical in outline, firmly fixed and not tender. It presented a marked expansile pulsation with a continuous coarse thrill, accentuated during systole. On auscultation, a loud continuous bruit with systolic accentuation, the typical "machinery murmur," was heard. The same type of murmur could be heard with less intensity over the dilated veins of the abdomen and even over those in the scrotum.

The second mass occupied the position of the lower half of the rectus muscles (Fig 1). This mass was firm, sharply defined, without pulsation, thrill or bruit, and without tenderness. It remained easily palpable when the rectus muscles were contracted and gave the impression of being superficial.

No other masses were felt, nor was the liver or spleen palpable. There were no signs of free fluid in the abdominal cavity.

The left leg was more swollen than the right (Fig 1). About the ankles and feet there was pitting edema, but in the calves and thighs the tissues were of brawny consistency and somewhat tender, presenting the typical characteristics of elephantiasis. The circumference of the right thigh was 57 cm, of the left thigh, 62.5 cm, of the right calf, 39.5 cm, and of the left calf, 33.5 cm. Over the anterior portion of the left lower leg was an area of scaly dermatitis. There was slight edema of the penis and scrotum.

The edema of the left leg was too marked to permit palpation of the arterial pulsations. The dorsalis pedis and the posterior tibial arteries were easily palpable on the right and the pulsations seemed of good quality. The systolic blood pressure in the right leg was about 20 Mm Hg lower than the pressure in the arms.

Laboratory Data and Special Examinations—The blood Wassermann and Kahn reactions were strongly positive. The red cell count was 3,440,000, and the hemoglobin 74 per cent (Dare). The white cell count was 8,200 with normal cell distribution. The urine presented occasional white blood cells and rare red blood cells. Phenolsulphonphthalein output was 70 per cent in two hours after intravenous injection. The blood from the enlarged left thoraco-epigastric vein showed an oxygen saturation of 55 per cent as compared with 23 per cent in the blood from the right basilic vein. Although these low readings are somewhat questionable as absolute values, yet, having been measured with the same apparatus and reagents at the same time, they are probably comparable. The venous pressure in the left thoraco-epigastric vein was 400 Mm of water, that in the left basilic vein 60 Mm of water. The P-R interval was 0.21 of a second, interpreted as being suggestive of heart disease.

The seven-foot roentgenogram of the chest showed the heart to be somewhat enlarged to the left, with possibly slight enlargement to the right. No abnormality of the thoracic aorta was seen. The width of the heart shadow was 58 per cent of the width of the bony thorax. Roentgenograms of the lungs and abdomen presented nothing remarkable. The lateral view of the lumbar spine revealed no evidence of bone erosion. A pyelogram, after injection of hippuran, revealed no abnormalities, except for slight displacement to the right of the right ureter at the level of the third lumbar vertebra.

Preoperative Diagnosis—A diagnosis was made of an arteriovenous fistula within the abdomen, involving the inferior vena cava and probably the descending aorta below the exit of the renal arteries. It was believed that the lesion was of spontaneous nature and was probably due to syphilis. The possibility of a preceding aneurysm seemed strong. The marked increase in symptoms in the preceding two weeks, the definite evidence of cardiac enlargement, and the absence of any other possible mode of attack

rendered surgical intervention inescapable, although it was realized that the chance of cure was remote

The patient received daily injections of bismuth for four days before operation. During the last 24 hours the patient was digitalized. Preparations were made for transfusion.

Operation—February 7, 1935. Under drop-ether anesthesia, a long right rectus incision was made. The subcutaneous tissue below the level of the umbilicus consisted almost entirely of a plexus of enlarged, distended, tortuous veins, the ligation of which was tedious and time consuming. On opening the abdominal cavity, no free fluid was found. Bimanual palpation of the firm mass in the lower abdomen revealed it to be within the abdominal wall and incision into it showed it to consist of a hard edema of the lower half of the rectus abdominis muscles, resembling elephantiasis (Fig 3). It was considered to represent the same changes in the rectus muscle as were present in the legs.



FIG 3—Photomicrograph from the rectus abdominis muscle (postmortem specimen) showing edema, fibrosis and cellular infiltration (Connective tissue stain)

An incision at the left of the root of the mesentery exposed the pulsating mass which consisted of a typical aneurysm about three inches in diameter. Over it, a marked, coarse thrill could be felt, which was transmitted downward into the region of the inferior vena cava and common iliac veins. The veins in the posterior abdominal wall were markedly dilated, including what was thought to be the spermatic vein.

In the superior wall of the aneurysm, a point of threatening rupture was apparent. It was, therefore, thought best to control the circulation entering the sac before further dissection. All the tissues in the neighborhood of the aneurysm were markedly inflamed and dissection was difficult. Tapes were placed about the abdominal aorta, the vena cava above the sac, and two vessels below the sac, which were considered to be the aorta and the vena cava. When the aorta above the sac was ligated (Chart 1), there was no drop in pulse, but the thrill disappeared and the blood pressure rose about 30

Mm Hg During the dissection, the weak point in the sac ruptured and had to be plugged with the finger After quadruple ligation, blood still escaped freely from the sac, and further dissection was attempted to find other entering vessels At this time it became obvious that the retroperitoneal tissues, distal to the sac, were thickened, edematous and scarred, presenting the pathologic appearance of elephantiasis, similar to that described in the legs and rectus abdominis muscles It was impossible to identify any structures, including even the larger vessels With increasing size in the accidental opening in the sac the situation became critical It was necessary to pack the sac with gauze, pressure upon which controlled all bleeding

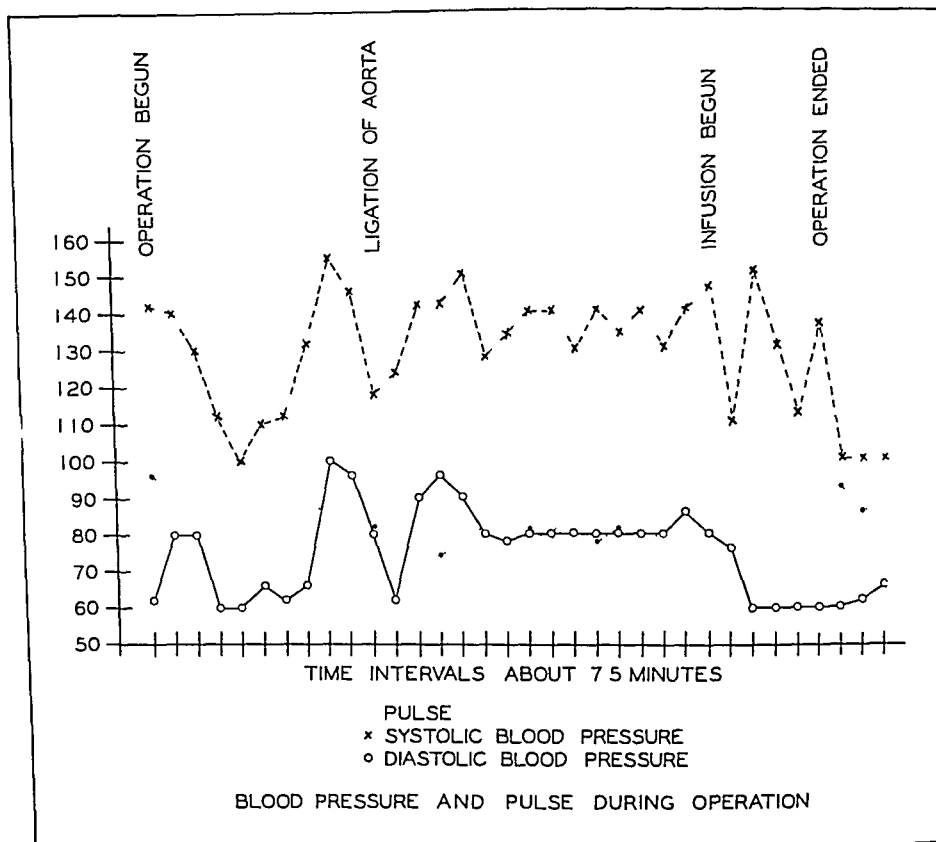


CHART 1—Showing the ranges of blood pressure and pulse rate during the operation. Note the absence of important changes particularly in the pulse rate and pulse pressure, after ligation of the abdominal aorta. Note, also, the absence of shock at the end of the operation, which lasted three and one-half hours.

Any attempt to remove the gauze resulted in the free escape of venous blood. The sac was, therefore, repacked and the abdomen was closed with silk. No stay sutures were employed, in order to avoid the possibility of obstructing the deep epigastric arteries as potential or actual collaterals.

During the operation the patient received 1,200 cc of normal saline solution. In spite of an operation lasting three and one-half hours and a considerable loss of blood, he was returned to the ward in excellent condition, with a pulse of 90 and a blood pressure of 130/60 (Chart 1).

Postoperative Course—Shortly thereafter, the blood pressure dropped to 100/60, and later numerous extrasystoles developed. At about this time there was a sharp rise in systolic blood pressure to 160, which was not sustained, the blood pressure shortly before death was 120/80. The patient died 15 hours after the end of the operation. After operation the patient voluntarily moved the feet and legs slightly, but during the last

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ten hours of life he was unable to move them. No venous pressures were obtained during the agonal period.

Autopsy—At postmortem examination, the heart was found definitely enlarged and hypertrophied. It weighed 490 Gm. The walls of both ventricles were somewhat increased in thickness. There was moderate dilatation of the right side of the heart and none of the left. There was no excess pleural fluid, but there was a slight degree of chronic passive congestion of the liver. Except for syphilitic aortitis, there were no other abnormalities related to the presenting lesion.

It was found that the fistula, measuring 1 cm in diameter, lay at the lower pole of an abdominal aneurysm, which involved the lower portion of the descending aorta from below the spermatic arteries to the bifurcation (Fig 4). The inferior vena cava was firmly attached to the wall of the aneurysm above the fistula and was markedly narrowed. The appearances suggested that there had been marked compression of the vena cava by the aneurysm preceding the occurrence of the fistula. The inferior mesenteric artery which had not been recognized at operation was found to originate from the posterior portion of the sac wall. The vessels that had been ligated were found to be the descending aorta and the inferior vena cava above the sac, and the two common iliac arteries below the sac. Without control of the inferior mesenteric artery, the lumbar arteries and the vena cava below the sac, the free bleeding after supposed quadrilateral ligation was readily explained.

The reason for the difficulty in identification of vessels also became apparent. On account of the retroperitoneal inflammatory tissue and edema, presumably the result of prolonged venous stasis, the pathologist could identify the vessels only after extensive dissection with the material removed from the abdomen.

In retrospect, it is believed that the patient suffered for about 18 months from compression of the inferior vena cava as the result of an aortic aneurysm. It is probable that perforation of the aneurysm into the vena cava occurred not more than 16 weeks, and possibly only two weeks, before admission. It is felt that such a large fistula, situated such a short distance from the heart, should have caused more marked cardiac symptoms and more apparent signs of cardiac failure unless the duration had been relatively short.

It is interesting that the ligation of the abdominal aorta was not associated with any immediate change in pulse rate, although there was a rise of 30 Mm Hg in systolic pressure. It is also interesting that, in spite of arterial control of the fistula, there was no immediate marked diminution of the pulse pressure.

It is probable that the condition was inoperable, although the necessity for an operative attempt was obvious. The difficulty encountered by the pathologist in identifying the vessels under favorable postmortem conditions

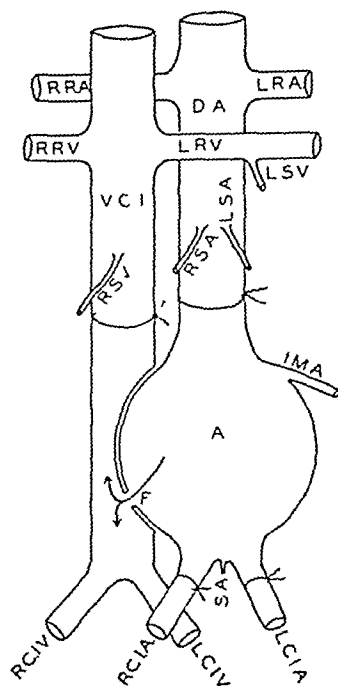


FIG 4—Diagram of actual conditions as found at autopsy. The position of the fistula and the compression of the proximal vena cava are indicated. The points of operative ligation are indicated. D A = descending aorta, V C I = vena cava inferior, R R A, L R A = right and left renal artery, R R V, L R V = right and left renal vein, R S A, L S A = right and left spermatic artery, R S V, L S V = right and left spermatic vein, A = aneurysm, I M A = inferior mesenteric artery, F = fistula, S = sac, R C I A, L C I A = right and left common iliac artery, R C I V, L C I V = right and left common iliac vein.

was so great, and the vessels that would have had to be identified and ligated for complete control of the fistula were so numerous, that, under relatively unfavorable operative conditions, the task became insuperable

The cause of death is not obvious. Shock or cardiac failure cannot be assumed in the face of an agonal systolic blood pressure of 120 Mm Hg

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CONGENITAL ARTERIOVENOUS FISTULA OR FISTULAE

CASE REPORT

PRESENTED, BY TITLE, IN DISCUSSION OF THE PAPER BY DOCTORS REID AND
MCGUIRE ON ARTERIOVENOUS ANEURYSMS

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Case Report—J D, white, male, age 33, was admitted to the Mercy Hospital, Baltimore, July 4, 1937. He complained of venous enlargements which extended from the left nipple line to the terminal point of the left foot and covered a corresponding area on the posterior surface. These varicosities were present on the left side only. He stated that the condition had existed since birth, and had neither diminished nor increased in severity or anatomic extent. He also complained of a slight limp, and occasional pain in the region of the varicosities. He has never at any time been incapacitated due to this condition. He had never had any serious illness in his life, other than the complaint mentioned. His family history was entirely negative.

Physical Examination showed a young man, lying comfortably in bed with no apparent discomfort. *Head* Scalp and ears negative, *eyes*—very nearsighted, both optic nerves normal, retinae normal, congenital myopia of seven to eight diopters in each eye, *nose*—breathing space rather limited and septum deviated to the right, *mouth*—teeth in rather good condition, two artificial teeth in lower jaw, all else negative, mucous membranes of good color. *Neck* No abnormal pulsations, no enlargement of vessels, a few small lymph nodes palpable on left side. *Chest* Lungs negative. *Heart* Apex beat was not visible or palpable. No abnormal thrusts, thrills or shocks. Percussion outline was clearly normal and apex within midclavicular line in fifth interspace. Auscultation—mitral sounds slightly muffled but no murmurs present. Aortic area negative. Pulmonic area negative. Pulse of equal force and rate, the latter remaining between 70 and 80 during his entire hospitalization.

General examination showed an enlargement of venous channels, both small and large, which was restricted entirely to the left side of the body. Anteriorly, the varicosities began about one inch above the nipple line and posteriorly at a corresponding level, sweeping around the left side of the chest. The venous enlargements were multiple, bluish colored, discrete and confluent. In the sitting or standing position, they became much more prominent. Anteriorly, they continued down over the left side of the abdomen and presented a number of large single dilatations. Posteriorly, there were no varicosities from the inferior angle of the scapula to the level of the crest of the ilium where they began to present a network of anastomosing vessels. The penis and scrotum were also affected, the dilatations being limited to the left side. The lower extremity was particularly affected. The left thigh, knee, leg, and especially the ankle, foot and toes on the left side were covered by a conglomerate mass of dilated vessels (Fig 1). There was no tenderness on palpation. The left side of the patient, from the nipple line down, was noticeably warmer to the touch than was the right side. There was no bruit heard, no thrill felt and no subjective sensation of thrill or throbbing. The skin over the right scapula was covered by a rather heavy growth of hair. This was not present on the opposite side. The upper extremities were not affected by venous enlargement. Blood pressure in both arms was 110/70. Pressure over the left femoral artery caused no change in heart rate. The reflexes in the lower extremities were active and equal. Muscle tone in the left lower extremity was much weaker than in the right. On palpation the muscles of the left lower extremity were much smaller and softer than corresponding

muscles on the opposite side. However, the left lower extremity was larger in circumference at almost every point than the right lower extremity. Five centimeters above the knee, the left thigh was 13 cm larger than the measurement at the corresponding point on the opposite side. The left knee was 2.5 cm larger than the right knee. Over the midpoint of the belly of gastrocnemius, the left side was 2.5 cm larger than the measurement at the corresponding point on the opposite side. The ankle on the left side was 5 cm larger than the right. The toes on the left foot showed hypertrophy of the cutaneous tissue, and each toe measured more in circumference than the corresponding toe on the opposite foot. The left lower extremity was 3.5 cm longer than the unaffected extremity. With the patient in the erect position, the left leg, ankle and foot became swollen and cyanotic and the vessels became markedly engorged.



FIG 1—Showing varicosities from above the left nipple line to the toes. (Infra red technique) Insert Same as Fig 1, with ordinary photography

directly into the bellies of the gastrocnemii. This thermocouple was originally designed for the measurement of internal temperatures of animals. It was used in conjunction with a sensitive galvanometer. The calibration of the thermocouple galvanometer combination was performed by immersing the two junctions in two beakers of water at different temperatures, these temperatures being read by thermometers. The sensitivity of the combination was found to be 70 Mm of deflection = 1 degree C, and 39 Mm of deflection = 1 degree F. Therefore, a difference in temperature could be measured to within about 1/70 of a degree C or 1/40 of a degree F.

Röntgenologic Findings—Left foot—swelling of soft tissues on dorsal and inner surface of foot. Bone atrophy with striation of both metatarsal and tarsal bones. No bone destruction or new bone formation. Left ilium—negative. Left femur and knee—marked striation. Left leg—marked forward and inward bowing of tibia with striation and numerous small areas of bone absorption. Bone not enlarged. Left fibula—enlargement with bending forward and inward, and rather marked striation with numerous areas of bone absorption throughout (Fig 2). Right tibia, fibula (Fig 3), femur, hip and ilium—no pathology shown.

* Two indirect methods used: (1) Gaertner's, and (2) modified Eyster's. Venous pressure was taken at corresponding points on each side with lower extremities in similar position.

Blood pressure variation in lower extremities

Arterial: Right popliteal region 130/78
Left popliteal region 156/100

Venous * the venous pressure was 40 Mm of water higher on the left side than on the right side

Temperature Variations

(1) Water bath immersion method: 2° F difference. The left foot consistently revealed a higher temperature than the right foot.

(2) Thermocouple determinations: Cutaneous, subcutaneous, and intramuscular temperature determinations of corresponding points on both sides showed that the left side registered a consistently higher temperature (Table I).

These temperature differences were measured by means of a copper constantan thermocouple, the junctions of which were mounted inside hypodermic needles. Temperature readings were obtained by placing the needles on the skin, subcutaneously and

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TABLE I

Region of Body	Inc Temp on Left*
I Ankle (surface)	2 1° F †
II Middle third of leg (surface)	
A Particularly venous region	2 3° F
B Region devoid of abnormal veins	0 4° F
III Intramuscular determination (gastrocnemius muscle)—1 inch below skin	1 2° F
IV Thigh (subcutaneous)	0 5° F
V Upper popliteal region (surface)	1 2° F
VI Posterior iliac region (subcutaneous)	1 1° F
VII Midaxillary region (surface)	0 4° F

* The degree of temperature difference between the right and left sides, or to what extent the left lower extremity and left side of chest and abdomen were warmer than corresponding points on the right side

† Temperature accuracy was to 1/70 of a degree centigrade or 1/40 of a degree Fahrenheit

FIG 2

FIG 3



FIG 2—Left or affected tibia and fibula See text for description

FIG 3—Right or unaffected tibia and fibula

Electrocardiographic Findings—Essentially normal tracing No evidence of any pathologic condition being present

Oxygen Determinations in Venous Blood of Right and Left Lower Extremities

(a) Blood taken at corresponding levels on both sides from venous channels

Right or Normal Side	Left or Affected Side
3 79 vol % or 49 9% O ₂ saturation	7 59 vol % or 100% O ₂ saturation
9 4 vol % or 39 6% O ₂ saturation	23 7 vol % or 100% O ₂ saturation
11 85 vol % or 47 5% O ₂ saturation	24 88 vol % or 100% O ₂ saturation

Therefore, the venous blood of the left lower extremity which is the one affected, has a higher O₂ concentration than the venous blood of the normal limb

(b) Venous blood on right side—bluish or dark red Venous blood on left side—bright red

Summary—Points substantiating a diagnosis of congenital arteriovenous fistula or fistulae

- (1) Visible venous enlargements on left side since birth
- (2) Increased venous pressure on left side
- (3) Venous blood of much brighter hue on left side than venous blood on right side
- (4) Higher O_2 saturation of venous blood on left side than O_2 saturation of venous blood on right side
- (5) Left lower extremity longer than right lower extremity Left lower extremity larger in circumference than right lower extremity at corresponding points
- (6) Temperature of left lower extremity approximately 2° F higher than right lower extremity
- (7) Left lower extremity shows some evidence of muscular atrophy
- (8) Bone atrophy, bowing, stunting and absorption on left side Slight degree of bone enlargement

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HEMINEPHRECTOMY IN DISEASE OF THE DOUBLE KIDNEY

REPORT OF FOURTEEN CASES

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IN THIS paper, we wish to present an analysis of 104 cases of double kidney, and, at the same time, to discuss the operation of heminephrectomy as a conservative measure in dealing with certain types of disease with this anomaly. We shall be able to illustrate this operative procedure by submitting a series of 14 cases in which heminephrectomy was the operation of choice.

The frequency of double kidney with complete or incomplete duplication of the ureters varies, according to different authors, from 12 to 10 per cent. It is generally stated that a conservative average for the incidence of this anomaly is 3 to 4 per cent of all autopsies. The anomaly may be unilateral or bilateral, with complete double ureters or bifid ureters. In view of the refinements in diagnostic technic which have been developed in recent years, it should be possible to study a case completely, so that therapeutic procedure can be decided upon in advance.

We have been able to collect a total of 104 cases of double kidney from the records of Mount Sinai Hospital. Analyses of this group are shown in the various appended tables.

TABLE I

Total Cases	Unilateral Double Kidney	Bilateral Double Kidney
104	89 (85.5%)	15 (14.5%)

TABLE II

Type of Lesion	Total	Right Side	Left Side	Double Ureter or Complete Duplication	Bifid Ureter or Incomplete Duplication	Symptoms	Showing Pathology	Upper Pole	Lower Pole	Both Poles	Operations
Unilateral double kidney	89	43	46	60 (67%)*	28 (31%)	51	48†	8	27	11	22
Bilateral double kidney	15	0	0	13	2	11	9‡	0	4	2	3

* In one case no information could be obtained as to duplication of ureter.

† In two cases pole not mentioned.

‡ In three cases no information as to the site of the lesion.

Of the 104 cases, there were 89 of unilateral double kidney (85.5 per cent), and 15 cases of bilateral double kidney (14.5 per cent).

Analyzing 89 unilateral double kidneys, 46 were found on the left side and 43 on the right side. Fifty-one cases had symptoms referable to the particular kidney, whereas, the 38 remaining had no symptoms. Sixty cases had complete duplication of the ureter (68 per cent), 28 cases showed incom-

plete duplication (31 per cent), and in one case information concerning this point could not be obtained. Forty-eight cases showed definite lesions (Table II). In 41 cases no definite lesion was discernible, the findings of duplication being made either at postmortem (24 cases) or clinically during routine examination. It is interesting to note that the kidney on the side opposite to the one which produced the presenting symptoms was found to contain a lesion in 17 instances.

TABLE III

Type of Lesion	Upper Pole	Lower Pole	Both Poles
Unilateral double kidneys	8 cases Calculus—3 Pyonephrosis—1 Ectopic ureter—2 Ureterocele—1 Hydronephrosis—1	27 cases Calculus—11 Pyonephrosis—9 Hydronephrosis—4 Tuberculosis—1 Carcinoma—1 Ureteritis cystica—1	11 cases Pyonephrosis—3 Pyelonephritis—3 Hydronephrosis—4 Infection—1
Bilateral double kidneys	No cases	4 cases Pyonephrosis—3 Infected hydronephrosis both lower poles—1	2 cases Pyelonephritis—1 Hydronephrosis—1

Of the 15 cases of bilateral double kidneys, 13 cases (87 per cent) showed complete duplication of the ureter on both sides. In the remaining two cases, the ureters were incompletely duplicated on both sides. There were symptoms in 11 cases. In four instances, the lesion was limited to the lower pole, in two instances both upper and lower poles were involved, and in three cases, no information was given as to the site of the lesion. Three of the cases were operated upon, two having a heminephrectomy and the third a complete nephrectomy. In six cases there was no definite lesion.

TABLE IV

TYPES OF OPERATIONS

Total number in both groups—25 cases
Heminephrectomy—14 cases
Complete nephrectomy—6 cases
Ureterolithotomy—3 cases
Pyelolithotomy—1 case
Cystoscopic cauterization of ureterocele—1 case

There were 62 patients in both groups who had symptoms. Of these, 25 cases were operated upon (Table IV). In other words, the incidence of symptomatology in all patients with a double kidney in our series was about 60 per cent, and operative therapy was carried out in 25 per cent of all cases, with or without symptoms. Braasch and Scholl¹ reported 30 operations in 144 cases (21 per cent). However, if the patient had symptoms referable to the kidney, the operative rate was 40 per cent. It is also of interest to note that of the 62 patients who had symptoms, 55 of these (90 per cent) showed

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definite lesions. An analysis of this series corroborates the impression that this type of anomaly predisposes the organ to serious pathologic changes, such as ordinary infection, tuberculosis, tumor formation, calculus and, most frequently, to obstructive conditions, leading to hydronephrosis or pyonephrosis (hydronephrosis or pyonephrosis was the lesion in 27 out of the 52 cases [52 per cent] in which the nature of the lesion was mentioned).

In the present series the predominance of pathology in the lower pole (31 out of 39 cases) is evident. This seems to be somewhat at variance with the incidence in the cases recorded in the literature as to the site of the lesion. It is readily accounted for by the fact that in many of those cases reported in

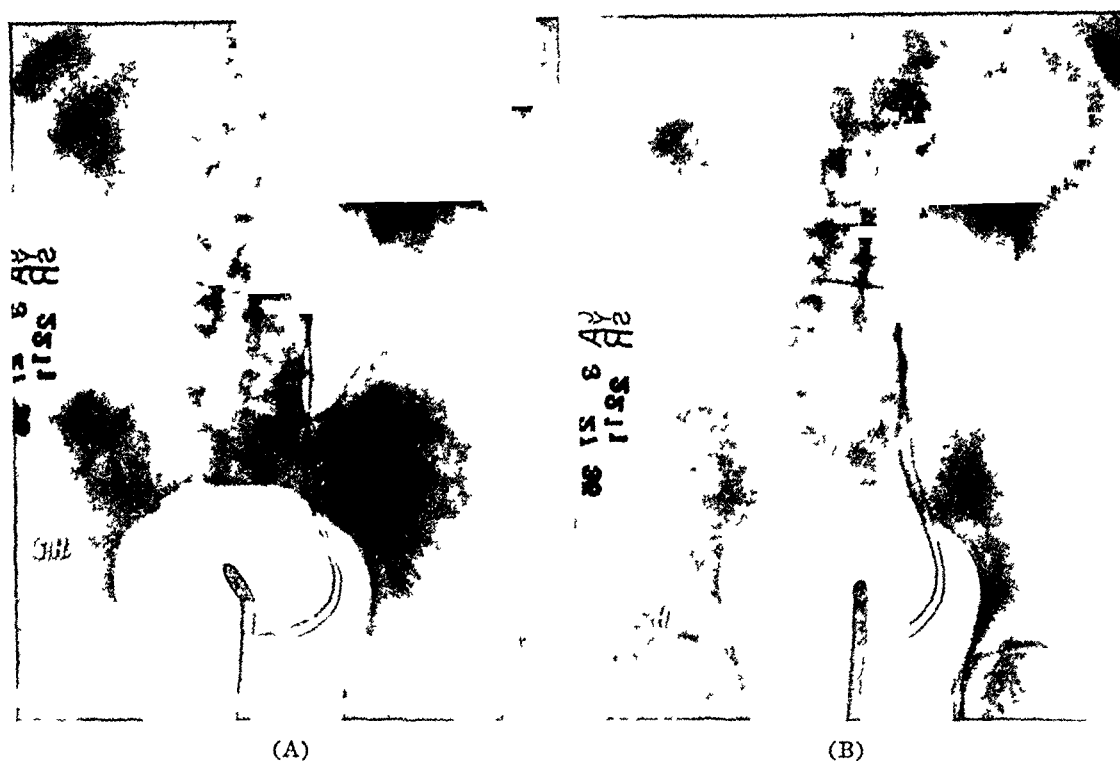


FIG 1—Tumor of the lower pole of a double kidney. (A) Retrograde pyelogram of the lower pole. (B) Retrograde pyelogram showing both pelvis.

which the upper pole contained the lesion were those of incontinence, in which an ectopic ureter opening was found. As is well known, these ectopic openings¹ always communicate with the upper pole. In our series, only two cases of ectopic ureter were present. In six of the 25 cases, in which operation was performed, heminephrectomy was contraindicated, and complete nephrectomy was necessary. In one case, a carcinoma was present in the lower pole (Fig 1A and B). In one case, there was a tuberculous process in the lower

* The one case in which the ectopic ureter communicated with the lower pole, as quoted by Moulonquet,⁸ may have involved a misinterpretation of the operative findings. In Case 14, for example, at the original nephrostomy operation, the mass apparently lay in the region of the lower pole, although subsequent events showed this to have been a huge pyonephrosis of the upper pole which, by sheer weight and size, had so overlapped the lower pole that the impression was gained that we were dealing with lower pole pathology. Since the operative details in M. Bourgeois' case are not recorded, it is best to withhold judgment until definite proof is afforded.

pole In the remaining four cases, the disease had either involved both poles, or there was little functioning renal tissue in the other half

Anatomy of Double Kidney—The two halves of the kidney may show distinct separation, as evidenced by shallow to deep grooving in the paren-



FIG 2—Case of complete duplication of kidney and ureters, showing communication between upper and lower pelves This was proven by injecting blue stained radiopaque solution through one of the two ureter orifices in the bladder and noting blue spurting through the other orifice At the same time, the above roentgenogram was obtained Further corroboration was obtained by placing one catheter in the second of the two left sided orifices and repeating the above procedure The results obtained were the same There was no history of previous disease of this kidney

chyma The external separation may extend into the interior and the two pelves may be completely separated, either by a band of renal parenchyma or by a fibrous septum Occasionally no external sign of demarcation between

the upper and lower poles may be noted. Instances have been reported in which wide separation has taken place between the two halves. Some of these fall into the class of true supernumerary kidneys. The existence of true intercommunication between the pelves has been denied by many, but Braasch,² Israel³ and Joseph⁴ have described such cases, and are agreed that true communication may exist. Mann⁵ (Fig. 2) and MacKenzie⁶ have each described this type of anomaly. Gruber,⁷ however, states that such intercommunication is due to fistulization, produced by gradual erosion of parenchyma, usually by stone.

The lower pole is usually the larger of the two halves. Its pelvis and caliceal system may be perfect in outline, whereas, the pelvis and calices in the upper pole are rudimentary and much smaller. Double kidney in one or both halves of a horseshoe kidney may occur, as in Case 4 (Fig. 4) in our series of heminephrectomized patients.

In cases where the ureter is completely duplicated, one should remember Weigert's law, namely, that the laterally placed ureteral orifice leads to the lower pole. The ureter to the upper half, in its uppermost course, may be close to the dilated pelvis of the lower diseased half. It may be displaced out of its normal position, or firmly adherent to the pathologic lower half. One must guard against injury to a ureter so located. Below, the ureters may be enclosed in the same sheath. If a diagnosis of duplication has not been made preoperatively, division of the normal ureter, as well as the one going to the diseased portion of the kidney, might result during the operation, involving the exposure of the lower half of the ureter.

The blood supply to the double kidney determines, in many instances, the feasibility of operative separation of the two halves. In most instances, two distinct sets of vessels supply the respective poles, in other cases the vessels to one pole may arise as branches from the vessels supplying the other pole. The ideal situation, from an operative standpoint, lies in the first anatomic disposition. The other anatomic arrangement contraindicates heminephrectomy.

Diagnosis of Double Kidney—With the advent of cystoscopy and pyelography by the retrograde and excretory methods, the diagnosis of the double kidney is made a relatively simple matter. The intravenous administration of a dye, such as indigo carmine, is of great aid in recognizing accessory ureteral openings, if their recognition should prove otherwise difficult. Uretro-pyelography by either method will be of help in those cases in which the ureters join before they reach the bladder. Suspicion of a double kidney should always be aroused when a small, incomplete pelvis, with minimal number of calices in the upper or lower portion of a kidney, is noted. What appears to be a ptosed kidney, without ureteral kinking on the same side, might be indicative of a lower pole of a double organ. Likewise, a pelvis, occasionally rudimentary and placed abnormally high under the ribs, might be indicative of the upper pole of a double kidney. The presence of an ectopic ureteral opening assures the investigator that he is probably dealing with a double

kidney and that the ectopic ureter leads to the upper pole. Patients suffering from such an anomaly are usually incontinent and can be cured of their incontinence by heminephrectomy, if the other half of the kidney is normal.

Heminephrectomy—There has been a tendency in renal surgery toward conservation of as much kidney parenchyma as possible. "Partial nephrectomy" or "partial resection" of the single kidney for localized hydro- or pyocalix, with suture of the remaining cut renal parenchyma, is an example of such an attempt at conservatism. The ideal situation for such procedure presents itself, of course, in the double kidney, in which a separate blood supply and pelvis exist for each of the two poles, as well as a partially or completely duplicated ureter. We shall employ the term "heminephrectomy," restricting its use to describe the operation in which a portion of the double kidney containing a separate pelvis is removed, after ligation of its separate blood supply and severance of its respective ureter. The terms "partial nephrectomy" or "partial resection" of the kidney should be reserved for procedures on the unduplicated organ. We exclude in this series those cases in which one-half of a horseshoe kidney has been resected.

Ionel⁹ collected, in the literature up to 1935, 52 cases in which heminephrectomy was performed. To these he added four of his own, in which the disease was pyelonephritis located in the upper pole. We have been able to collect 30 additional cases in the literature^{10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 32} up to 1938, bringing the total up to 86 cases reported. To these we wish to add 14 of our own cases from the records of Mount Sinai Hospital, making a total of 100 cases in the literature at the present time.

An analysis of these 100 cases shows that in 51 instances the disease for which the operation was performed was in the upper pole, 37 in the lower pole, and in 12 no mention was made as to the site of the lesion. In the 51 upper pole cases are included a fair number of instances in which an ectopic ureter opening was found. Almost invariably, this ureter leads to the upper pole.

TABLE V
TOTAL COLLECTED CASES OF HEMINEPHRECTOMY

Period	Total	Upper Pole	Lower Pole	No Information
Cases up to 1935	56	26	25	5
Cases 1935-1938	30	21	2	7
Present series	14	4	10	0
Total	100	51	37	12

Indications and Contraindications for Heminephrectomy—It can be stated that heminephrectomy may be performed upon double kidneys in which one segment is involved in a hydro- or pyonephrotic, calculous or infectious process, providing one of the following conditions or situations is not present:

(1) Tuberculosis. Here the tuberculous process very frequently involves the parenchyma of the other pole. However, Legueu²³ and Heymann²⁴ have each reported one case in which heminephrectomy was performed upon a

double, solitary kidney with good results. We might modify the indication in these cases by stating that where the kidney is solitary and there is no involvement of the other half, the procedure is justified.

(2) Malignant tumors are contraindications to this procedure. In the series, we referred elsewhere to a case in which there was a tumor in the lower pole.

(3) Nonfunction of the remaining portion of the kidney.

(4) Single blood supply to both poles.

(5) Technical difficulty in separating the two halves of the kidney.

(6) Advanced disease of both halves (mild infection in one-half is not a contraindication) and especially hematogenous infection.

(7) Communication between the two pelves.

Operative Technic—The various points in the technic of heminephrectomy, as practiced on our service, may be summarized as follows:

(1) Exposure of the kidney through a loin incision. Occasionally, where the upper pole is the one to be removed, and the kidney is situated at a high level, resection of the twelfth rib may be necessary. The extent of mobilization of the kidney should be minimal, because of the danger of rupture of aberrant vessels necessary for the nourishment of the remaining part of the kidney.

(2) Exposure of the ureters and tracing of their course to the respective poles.

(3) Exposure of the blood supply to both halves and notation of its distribution. The operation will depend a great deal for its success upon whether or not the blood supply to the remaining half of the kidney is adequate.

(4) Location of a line of separation of the two halves.

(5) Ligation of the respective ureter. It is to be remembered that the two ureters very often lie in the same sheath. Separation of the two ureters, without injury to the one going to the remaining half, is essential. If the ureter is normal, the point of ligation should be as low as possible. In those cases, however, in which the ureter is markedly diseased and dilated, complete ureterectomy is preferable. The lowermost portion of the ureter may be isolated and divided close to the bladder by continuing the original lumbar incision, or by making a separate incision in the lower quadrant of the abdomen, identifying the ureter by pulling gently on the freed ureter above. Where the ureter is ligated at the bladder, it is essential to prevent "blowout" of the tied stump postoperatively, by keeping the bladder relatively empty for a number of days by employing an indwelling catheter or by catheterization at regular intervals. Division of the ureter is accomplished by the carbolized knife. In those cases in which there has been a separate incision for juxtavesical division of the ureter, it is best to prevent contamination by covering the proximal stump with a finger cot before pulling the ureter along the tract leading to the lumbar incision. In the case of the "Y" ureter, the ligation should be made a short distance above the junction of the two ureters. The reason is obvious.

(6) Ligation of the blood supply to the portion of the kidney to be removed may cause a blanching of the parenchyma, which will aid in locating the zone of demarcation between the upper and lower poles. Delineation of a separation zone is aided in many cases by inserting a finger into the diseased pelvis and using this as a guide in dividing the upper from the lower pole.

(7) After removal of the diseased portion, mattress sutures, underpinned with fat, muscle or fascia, according to the Beer technic,²⁵ may be employed to secure hemostasis and at the same time to suture the cut ends of the remaining tissue.

(8) Rubber dam drain and closure of the wound.

Variations in Technic—Von Lichtenberg²⁶ decapsulates the diseased portion after ligating the vessels. He notes the blanching in the portion deprived of its blood supply before making the separating incision. This obviates compression of the vessels to the healthy portion, as practiced by some. The decapsulated flaps are inserted into the wedge shaped cavity at the point of resection. Lennander,²⁷ Wright²⁸ and others perform nephropexy of the remaining half (usually lower pole). Lowsley²⁹ employs ribbon-gut for approximation of the cut edges of renal parenchyma. Miller³⁰ and Hicks¹⁸ both ligated the ureter to the diseased portion of the kidney in an attempt to cause atrophy, since, in the two cases reported, heminephrectomy was not feasible. In Miller's case the upper pole of the right kidney was diseased, and at operation only one renal vascular pedicle was present. He resected 5 cm. of the upper ureter and ligated the stump. The patient made an uneventful recovery. In Hicks' case, there was a hydronephrosis in the upper half. The patient's chief symptom was pain. The ureter to the upper half was ligated, in the hope that atrophy would occur, but there was no relief from the pain. At a second operation, an heminephrectomy was performed.

CASE REPORTS

Case 1—L. A., female, age 29. *Diagnosis* (1) Complete duplication right kidney and ureter. (2) Pyonephrosis lower half. *Operation* Right heminephrectomy and ureterectomy. *Result* Well.

The patient gave a history, extending back six years, of pain in the right kidney area, associated with frequency, pyuria, hematuria and dysuria. Cystoscopic and pyelographic studies revealed a single, normal kidney on the left side, a completely duplicated kidney and ureter on the left side, and a pyonephrosis of the lower half of the double kidney. The upper pole of the double kidney was normal (Fig. 3A and B).

Operation—July 19, 1932. Heminephrectomy, lower half, and complete ureterectomy (E. Beer). The right kidney was exposed. The upper half was distinctly divided from the lower half and appeared grossly normal, and a normal ureter appeared from this pole. The lower half of the kidney was hydronephrotic and the ureter was dilated. Both ureters were followed down for a considerable distance and freed. They were both contained in the same sheath. The lowermost ends of the ureters were exposed through a separate incision in the right lower quadrant of the abdomen. The dilated lower ureter was ligated and severed about 1½ cm. from its entrance into the bladder. The proximal ureteral stump was covered with a finger cot and then drawn through the track and out.

HEMINEPHRECTOMY

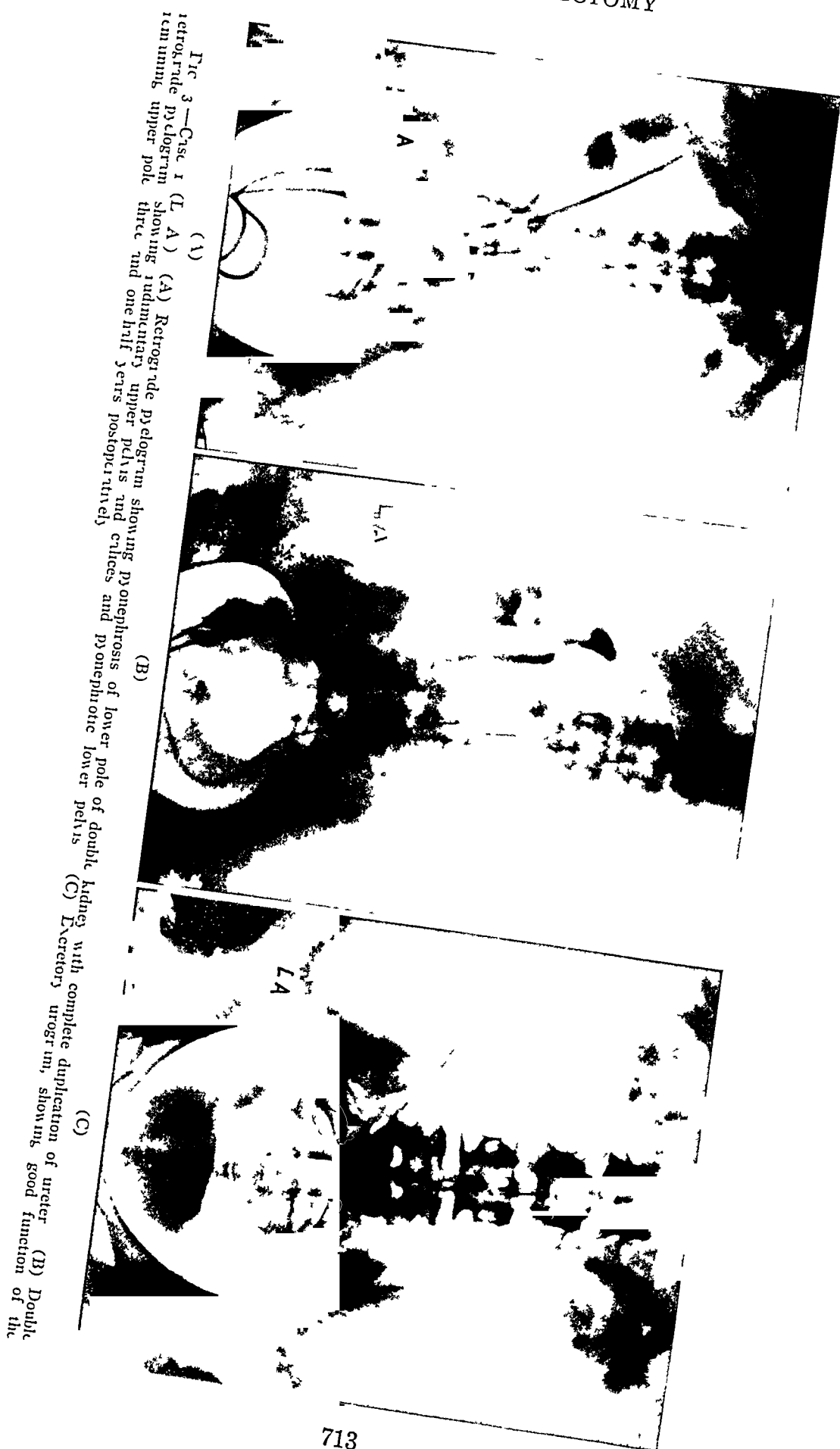


Fig 3—Case 1 (L A) (A) Retrograde pyelogram showing pyonephrosis of lower pole of double kidney with complete duplication of ureter. (B) Double excretory urogram, showing good function of the kidneys. (C) Retrograde pyelogram showing indurated upper pole three and one-half jets postoperatively.

through the lumbar incision. The two halves of the kidney were then separated and the lower pole with its ureter removed.

Following operation there was some urinary leakage from the lumbar incision. Leakage also occurred from the anterior wound. This ceased after introducing an indwelling ureteral catheter, the patient was discharged with both wounds firmly healed.

Follow-Up—December 28, 1935 (three years later). There was good function of the remaining upper pole of the right kidney, as evidenced by excretory urography (Fig 3C).

Case 2—A T, male, age 40. *Diagnosis* (1) Double right kidney with partial duplication right ureter. (2) Dendritic calculus lower pole. (3) Right hydronephrosis (both halves). *Operation* (1) Right pyelolithotomy and nephrostomy (lower pole). (2) Right heminephrectomy (lower pole). *Result* Well.

This patient entered the hospital August 29, 1933, complaining of right loin pain, frequency and pyuria of eight months' duration. There had been no chills or fever. His past history disclosed two cystolithotomies performed 21 and 15 years previously, and an incision and drainage operation for a left perinephritic abscess 13 years previously. Examination disclosed a pale individual. The right kidney was palpable and tender. The urine contained numerous white blood cells. Blood urea was 75.0 mg per 100 cc, hemoglobin 55 per cent. Roentgenologic examination showed a dendritic calculus on the right side and a hydronephrotic, very much deformed pelvis on the left. Roentgenograms taken with the catheter in situ on the right side disclosed the tip of the catheter to be in contact with the calculus at the 25 cm level. There was no flow of urine from this side. On the left side the excretion and function were poor. The azotemia was treated vigorously. Apparently the patient had a very much damaged kidney on the left side and a blockade on the right. It was felt his only chance lay in removing the calculus on the right side. Accordingly, despite the poor condition of the patient, the dendritic calculus was removed piecemeal through pyelotomy and nephrotomy incisions. Control roentgenograms taken on the operating table revealed no further calculi. A drainage tube was placed in the pelvis through a nephrostomy opening.

Postoperatively, the blood urea rose to 168.0 mg, and after intensive treatment the azotemia gradually cleared up. The patient drained moderately large amounts of urine through the nephrostomy tube. Blue was injected into this tube to determine the patency of the ureter, but none appeared in the bladder urine. This indicated some obstruction, and with this in mind, cystoscopy was performed. The right and left ureters were catheterized to the pelvis, good indigo carmine excretion was obtained from the right side (catheter apparently in the upper pole). Concentrated blue solution injected through this catheter did not appear through the nephrostomy tube. Blue coloration from the left side was definitely weaker than that obtained from the right, contradicting previous functional tests. A suspicion of a right double pelvis was entertained. This was confirmed when pyelograms were made singly and simultaneously and at different times, by injecting radiopaque solution through the right ureteral catheter and through the nephrostomy tube. About this time, the patient suddenly passed a small, almond sized stone. It was felt that this may have represented a portion of the original calculus which had broken off and had obstructed the flow from the nephrostomized lower pole. Indigo carmine solution was instilled through the nephrostomy tube, but did not appear in the bladder. The nephrostomy tube was inadvertently removed, and it was necessary to reoperate upon the patient and to renephrostomize the kidney. At this operation, it was impossible to thoroughly explore the entire region, and to demonstrate a double ureter. Heminephrectomy was considered at this operation, but it was felt the patient probably could not undergo such a formidable procedure and that we would have to be satisfied with a permanent nephrostomy. His blood urea remained at about 35.0 mg. Apparently the strongest functional element in his excretory system was the upper pole of the right kidney.

Follow-Up—He was discharged with the nephrostomy tube in place. Three months

later he returned to the hospital because of some trouble he was having in caring for the nephrostomy tube and its drainage. Studies showed practically no function from the lower half of his right kidney. In view of his better general condition and practically normal blood urea, it was decided to perform a heminephrectomy of the lower half of the right kidney.

Operation—March 27, 1934. Heminephrectomy (A. Hyman). The right kidney was found densely adherent as a result of the two previous operations. The kidney was, however, eventually mobilized. It was impossible to expose the ureter. Somewhat more than the lower half of the kidney was resected and hemostasis effected by chromic sutures underpinned with fat. The patient was discharged 26 days after operation.

Follow-Up—After discharge the patient developed urinary leakage from the wound, which has persisted, despite all local measures. It was felt the leak was caused by retained cortical renal tissue. Cystoscopy soon after discharge from the hospital (August, 1934) showed good indigo carmine excretion from the right kidney. An excretory urogram, taken in August, 1936, showed insufficient visualization for diagnostic purposes on both sides.

Case 3—D. A., female, age 40. *Diagnosis* (1) Double right kidney and partial duplication of right ureter. (2) Pyonephrosis and hydro-ureter, lower half. *Operation* Heminephrectomy, lower half of right kidney. *Result* Well.

Ten years previously, this patient had had colicky pains in the right lumbar region. Nine years ago, a right ureterolithotomy was performed. Seven years later, there was a recurrence of right-sided pain, pyuria and frequency of urination. On cystoscopy a single right ureter orifice was seen, and there was a temporary obstruction to the passage of a ureteral catheter at 9 cm, where a retention of 80 cc of pus was found. At the 29 cm level there was a retention of 20 cc of pus. Retrograde pyelography revealed a duplicated right kidney with a normal, small upper pelvis and markedly dilated lower pole.

Operation—Heminephrectomy (right lower half) and partial ureterectomy (L. Edelman). The lower pole was cystic, the pelvis was dilated and the ureter was one inch in thickness. The upper pole ureter appeared normal. There were two distinct sets of vessels going to both halves of the kidney. The dilated ureter was fixed in the bony pelvis to a cystic structure, which was probably an intraligamentous cyst. The ureter was ligated one inch from the bladder, where its diameter measured one-quarter of an inch. The actual site of the bifurcation could not be determined, because of the intimate relationship with the cyst. The lower portion of the kidney was then resected. The bleeding was readily controlled by a few mattress sutures of chromic gut.

Recovery was uneventful. It has been impossible to obtain a follow-up on this patient.

Case 4—L. G., male, age 44. *Diagnosis* (1) Horseshoe kidney. (2) Complete duplication of left half of horseshoe kidney. (3) Hydronephrosis upper half left kidney. (4) Pyonephrosis lower half left kidney. *Operation* Heminephrectomy, lower half left side of horseshoe kidney. *Result* Well.

The patient was admitted with a three weeks' history of left renal colic, associated with chills, fever, hematuria and pyuria. On examination, a large, smooth, tender mass was felt on the left side of the abdomen, extending from the free border of the ribs to the crest of the ilium. At cystoscopy the right ureter orifice was found to be normal. On the left side two ureteral orifices were present. All three ureters were catheterized without obstruction. There was thick, purulent urine coming from the left lower kidney, the function of which was very poor.

Operation—September 10, 1912. Heminephrectomy lower half left side of a horseshoe kidney (L. Buerger). A large, multilocular, pyonephrotic sac, adherent to the peritoneum and involving the whole lower half of the left kidney, was found. The upper half of the left kidney represented the left half of a horseshoe kidney (Fig 4). The sac contained two quarts of purulent material. The upper pole presented a hydronephrotic pelvis with good renal parenchyma. There were two ureters. The pyonephrotic half

of the left kidney was excised. At first the upper ureter was ligated and cut, with the intention of removing the entire left kidney, but due to the excellent condition of the parenchyma in the upper pole, it was decided to attempt to conserve this pole. Accordingly the cut upper ureter ends were anastomosed over a No 6 F₁ ureteral catheter. The patient had some urinary leakage through the lumbar sinus.

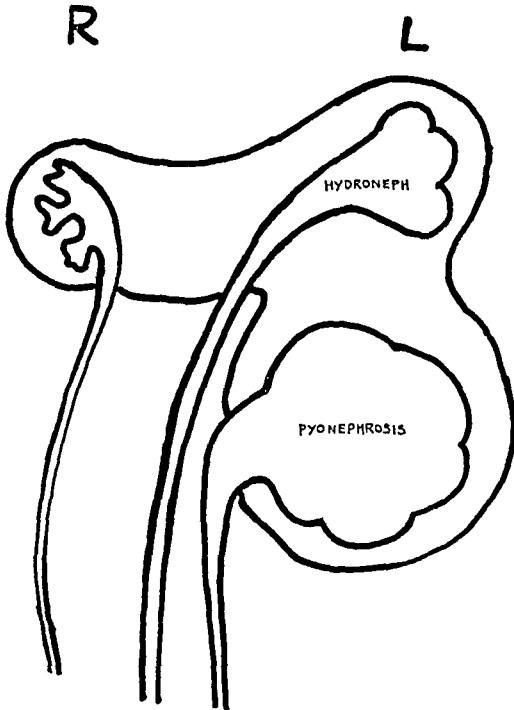


FIG 4—Case 4 (L. G.) Schematic drawing of operative findings in a case of horseshoe kidney with complete duplication of its left half which joins the right kidney by the upper pole.

Follow-Up—At cystoscopy, performed one month later, only a few drops of urine were obtained from the upper pole. There was also a trace of indigo carmine from the lumbar wound after 40 minutes.

The patient was still alive, about 17 years later, although no functional studies of the remaining upper pole have been made.

Case 5—N. R., male, age 44. *Diagnosis* (1) Double kidney (left) with partial duplication of the ureter. (2) Calculus, hydronephrosis left upper pelvis. *Operation* Heminephrectomy, upper pole left kidney. *Result* Well.

In 1906, patient had a cystolithotomy performed. For five years previous to admission to the hospital, he complained of bilateral sacral pain with recent radiation along the left thigh. There were no urinary symptoms. Cystoscopic and pyelographic studies revealed a double left kidney and partial duplication of the ureter, with calculous hydronephrosis of the upper pelvis (Fig 5A and B).

Operation—August 18, 1931. Heminephrectomy for calculous hydronephrosis, left upper pole (E. Beer). The kidney was found to be about one-third larger than normal and surrounded by adherent fat. Two ureters were exposed and found to unite three inches below the lower pole of the kidney. The lower ureter was normal, the upper ureter contained a stone at the level of the lower pelvis. It was thickened, as was the pelvis. The vessels were exposed, and it was noted that the branches to the upper third of the kidney apparently came off the main vessels. These upper branches were ligated. The parenchyma of the upper pole was reduced to about one third the normal amount and the pelvis was hydronephrotic. After ligating the vessel branches, the upper third of the kidney was cut across about 1 cm above the groove which separated the healthy part from the hydronephrotic third. Bleeding was controlled with hemostatic sutures and the beveled edges of the kidney incision were brought together with chromic sutures, underpinned with fat. The upper ureter was tied 1 cm above the bifurcation and removed in one piece, with the hydronephrotic pole. Except for a mild wound infection, the patient made a good recovery.

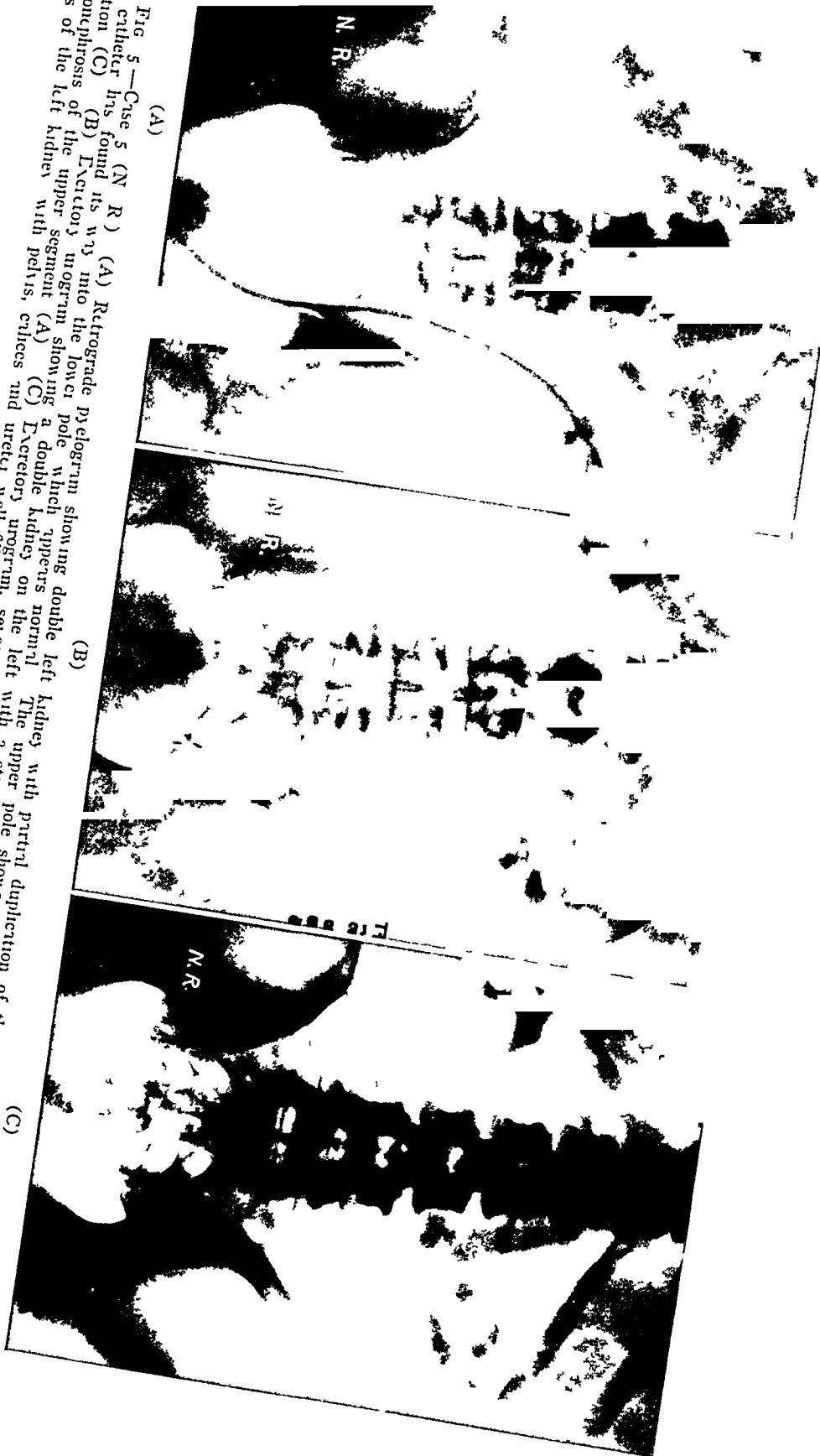
Follow-Up—An excretory urogram, May 21, 1938, seven years after operation, showed good function of the remaining lower half of the left kidney (Fig 5C).

Case 6—L. F., female, age 42. *Diagnosis* (1) Complete duplication left kidney and ureter. (2) Nephrolithiasis, lower half. *Operation* Left heminephrectomy, lower half. *Result* Died.

This patient had had recurrent attacks, over a period of eight years, of right lumbar pain associated with frequency, urgency and pyuria. She thought she had passed a small stone six months previously. Three months later she began to complain of left lum-

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Fig 5—Case 5 (N R) (A) Retrograde pyelogram showing double left kidney with partial duplication of the ureter (one orifice in bladder) junction (C) (B) Evacuity urogram showing a double kidney on the left with a stone at the ureteropelvic junction of the upper pelvis and a third of the left kidney with pelvis, calices and ureter well filled (C) Evacuity urogram, seven years postoperatively, showing good function of the conserved lower two



bar pain and hematuria. Roentgenologic examination demonstrated a large concretion about 1 cm in size in the region of the lower pole of the left kidney. Cystoscopic and pyelographic studies showed a completely duplicated left kidney and ureter with a calculus in the lower pelvis.

Operation—August 26, 1926. Heminephrectomy, left lower half for calculosis (P. W. Aschner). The kidney was partially divided into upper and lower half. A large stone and considerable sandy deposit were found in the lower half of the kidney. There were two sets of vessels, each going to the respective poles of the kidney. The lower half of the kidney was opened through a nephrotomy incision. The stones and sand material were removed, and the pelvis irrigated. In view of the presence of considerable sand material and the unlikelihood of successfully removing all of it, an heminephrectomy was

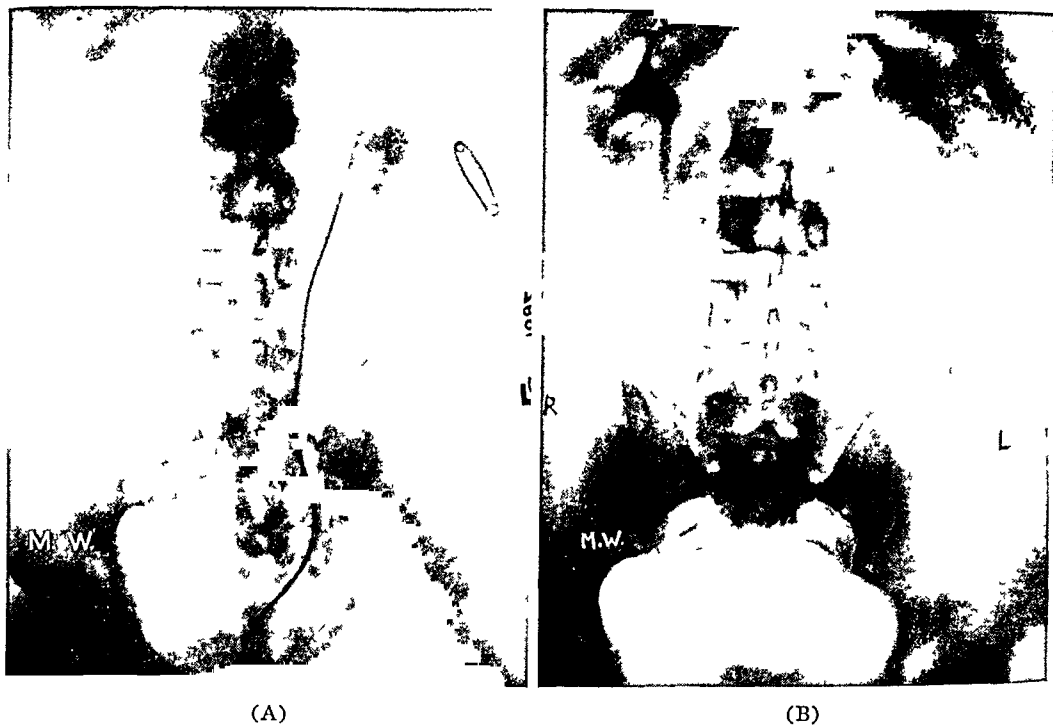


FIG. 6—Case 7 (M. W.). (A) Complete duplication left kidney and ureter. Pyelogram showing pyonephrosis of lower half. The second ureter not catheterized because of good function after injection of indigo carmine. (B) Excretory urogram six years postoperatively, showing good excretion from remaining upper segment, pelvis of which is small and leads into a normal appearing ureter.

performed, during which procedure an aberrant vessel to the upper pole was injured and bled profusely. The hemorrhage was finally controlled by a hemostat, which was left in place, and the lower part of the kidney was resected. The patient lost a considerable amount of blood, she was returned to bed in shock, from which she died three hours later, despite all measures to combat this condition.

Case 7—M. W., male, age 26. *Diagnosis* (1) Complete duplication left kidney and ureter. (2) Pyonephrosis lower half (aberrant vessel). *Operation* (1) Left nephrosotomy, lower half. (2) Secondary heminephrectomy, left lower half. *Result* Well.

For three weeks, the patient had complained of left lumbar pain and dysuria. The urine, which was said to have been clear at first, later became turbid, and a temperature of 103.8° F developed. On physical examination there was found a ballotable, tender mass in the left lumbar region. There was definite costovertebral tenderness on this side, and roentgenologic examination revealed a curvature of the spine, with the convexity toward the right. The urine was loaded with pus. Excretory pyelography showed a normal kidney on the right side. The left pelvis and calices were deformed and the left ureter appeared compressed in its upper half. At cystoscopy two ureter orifices

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were found on the left side. The lateral one (lower pole) was slightly edematous. Milky fluid was seen discharging from this orifice. The lateral ureter was catheterized for 20 cm, where an impassable obstruction was encountered. There was no flow at this level. The mesial ureter orifice (upper pole) appeared normal, good indigo carmine efflux was seen, and it was not catheterized. A diagnosis of pyonephrosis of the lower half of a double kidney was made (Fig 6A).

Operation—December 12, 1931. Nephrostomy of a pyonephrotic lower half of a left double kidney (E. Beer). There was extensive perinephritis surrounding the lower pole. The lower pole, comprising about two-thirds of the kidney, was composed of three calices and had been converted into a sac. The ureter to the lower half was the size of a pencil. No calculus was present. The ureter could not be probed from above.



FIG 7—Case 8 (S. S.). (A) Retrograde pyelogram showing complete duplication with rudimentary upper pelvis and calculous pyonephrosis of lower pole right kidney. (B) Excretory urogram, six years postoperatively, showing good function of remaining upper pole, right kidney.

There were about eight ounces of pus in the pyonephrotic sac. The exact cause of obstruction to the ureteral catheter at cystoscopy could not be determined.

Postoperatively, there was very little discharge through the nephrostomy wound. Blue stained fluid instilled into the lower pelvis through the nephrostomy tube did not appear in the voided urine, indicating some form of blockade. Catheterization of this ureter and instillation of blue stained fluid did not show any flow out of the nephrostomy tube, but after digitally opening into the lower pole, there was copious flow of blue fluid. Iodide was instilled into the lower pole and a large dilated pelvis was outlined. No iodide passed down into the ureter. There was a defect at the ureteropelvic junction, suggesting an aberrant vessel. Excretory urography showed no excretion from this pole.

Second Operation—January 2, 1932. Subcapsular heminephrectomy for pyonephrotic sac of lower pole (E. Beer). On delivering the sac, two groups of vessels were exposed going to the lower pole, and a branch apparently crossing the ureteropelvic junction and occluding same was found. The sac was the size of a peach, and the amount of renal parenchyma reduced. The ureter was small. The patient was discharged from the hospital well.

Follow-Up—In January, 1938, six years after operation, excretory urography showed good function of the remaining upper pole (Fig 6B)

Case 8—S S, male, age 47 *Diagnosis* (1) Complete duplication right kidney and ureter (2) Renal calculus and pyonephrosis lower half *Operation* Heminephrectomy, lower half right kidney *Result* Well

Fifteen years previously this patient had had a suprapubic cystolithotomy performed. Eight years later, he developed a right renal colic and since then has had repeated attacks. During the year before his present admission, the pain has been persistent. He noted hematuria on one occasion. Cystoscopic and pyelographic studies showed a single normal kidney on the left side. The right kidney and ureter were completely duplicated. The lower half was filled with stones and was moderately dilated. The upper half was also dilated (Fig 7A).

Operation—February 5, 1932 Heminephrectomy, lower pole right kidney for calculus pyonephrosis (E Beer). There were considerable perinephric and peri-ureteral adhesions. The lower ureter was moderately thickened. A large artery crossed posteriorly to the lower ureteropelvic junction, toward the lower pole. After evacuating many stones and much sand from the lower pelvis and calices, only a shell of kidney parenchyma was found in the lower pole. The upper half of the kidney had good parenchyma and the upper pelvis was found to be small. The lower ureter was isolated and ligated. After sectioning it, and the aberrant vessel at the ureteropelvic junction, the lower pole was resected. Three mattress sutures were used to control the slight ooze and to close the lower resected edge. Except for a wound infection, the patient made an uneventful recovery and was discharged well.

Follow-Up—In April, 1938, six years later, excretory urography showed good function of the remaining upper pole (Fig 7B).

Case 9—M O, male, age 23 *Diagnosis* (1) Bilateral complete duplication of kidneys and ureters (2) Hydronephrosis right upper pelvis (3) Atrophy right kidney (4) Left hydronephrosis and hydro-ureter, lower pole *Operation* (1) Right complete ureteronephrectomy (2) Heminephrectomy, lower pole left kidney *Result* Well

The patient was first seen in 1922, with a history that for a period of two years he had been complaining of bilateral lumbar pain, frequency, urgency, and burning on urination. A complete nephrectomy of a double right kidney and ureter was performed at that time. The entire kidney was found atrophic. The upper pelvis was dilated, due to a valve-like obstruction in the upper ureter. In view of the atrophy of the entire organ, complete nephrectomy and ureterectomy was performed, June 22, 1922, by Dr A Hyman.

The patient was again admitted to the hospital, in 1927, complaining of persistent pyuria since his previous discharge from the hospital. There was also dull, left lumbar pain. Cystoscopy showed four ureter orifices. The left lateral ureter (lower pole) was edematous and obstructed at 1 cm. The left mesial orifice (upper pole) was catheterized to the pelvis. A retrograde pyelogram of the upper pole showed a triangular shaped area of upper pelvis with two or three calices. No pyelogram could be obtained of the lower pole.

Operation—October 14, 1927 Heminephrectomy and partial ureterectomy, lower half left kidney (A Hyman). The upper half of the kidney appeared normal. The lower half was a hydronephrotic sac. There was a definite line of fusion across the middle of the kidney. The upper ureter was normal. The lower ureter was thickened and dilated to the size of a thumb. The lower pelvis was opened and a finger introduced into the calices, to demarcate the limits of the lower half. Because of bleeding, some mucosa was left behind. Mattress sutures, underpinned, were employed to control the bleeding.

Subsequent Course—Postoperatively, the patient developed uremia and psychosis and an infected wound, from which he gradually recovered after intensive treatment. He has

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remained well since then for the past 11 years, with normal blood urea. At present he is living on *approximately one-sixth of the normal amount of kidney parenchyma*.

Case 10—J G, female, age 14. *Diagnosis* (1) Bilateral, complete kidney and ureteral duplication. (2) Pyonephrosis of lower half left kidney. *Operation* Heminephrectomy, lower half left kidney. *Result* Well.

The patient had complained of attacks of "pyelitis," associated with pyuria and fever since birth. After a number of years of investigation by numerous urologists, her case was finally diagnosed as one of complete bilateral kidney and ureter duplication, with the focus of her pyuria located in a pyonephrotic lower half of the left kidney.

Operation—September 29, 1937. Heminephrectomy of the pyonephrotic lower half of the left kidney (E Beer). Lower half of left kidney found to be markedly adherent.

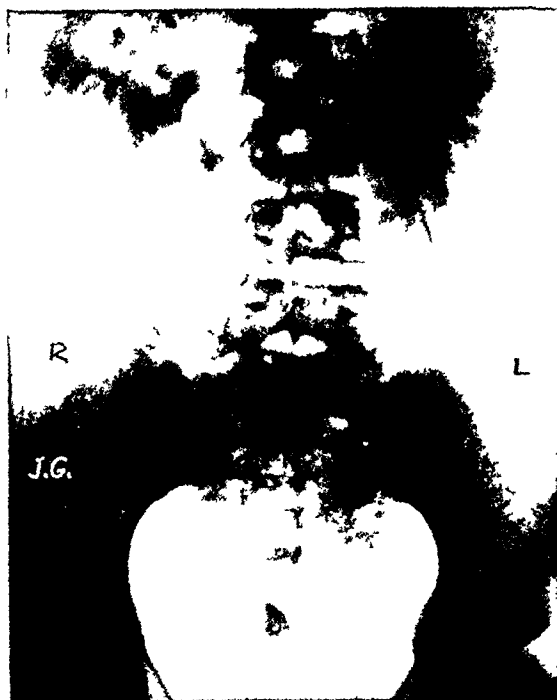


FIG 8



FIG 9

FIG 8—Case 10 (J G). Excretory urogram showing good function in the remaining upper segment of left kidney seven months after heminephrectomy of lower half of left kidney for pyonephrosis.

FIG 9—Case 11 (R W). Excretory urogram showing good function from remaining upper segment left kidney one and one half years after removal of left lower pole for pyonephrosis.

The ureter to the lower half was dilated and thickened. Several aberrant vessels were found, and these apparently contributed to the causation of the pyonephrosis. The renal cortex in the involved pole had practically disappeared, so that this portion of the kidney was converted into a sac. The upper pole contained good renal parenchyma. Because of the extreme thinness of the pyonephrotic sac, it was inadvertently opened during the separation of it from the upper pole. The contents of the sac were evacuated and the sac wall removed by sharp dissection and curettage. The ureter was divided low.

Subsequent Course—Postoperatively, the wound became grossly infected. It was widely opened and allowed to heal by secondary intention. No hernia of the wound has occurred thus far. Excretory pyelography, eight months later, showed good function in the remaining upper pole (Fig 8).

Case 11—R W, female, age 8. *Diagnosis* (1) Complete duplication of left kidney and ureter. (2) Pyonephrosis of lower half left kidney. *Operation* Left uretero-heminephrectomy, lower half. *Result* Well.

For two weeks prior to admission to the hospital, the child complained of left loin pain and dysuria associated with cloudy urine and temperature, reaching as high as

105° F On physical examination, the outstanding physical sign was left costovertebral angle tenderness At cystoscopy, two left ureteral orifices were found, and a diagnosis of pyonephrosis of the lower half of the left kidney was established

Operation—July 3, 1936 Left, complete ureteroheminephrectomy of the lower half (E Beer) The operation was carried out through a left loin and an anterior abdominal incision By employing the two incisions it was possible to accomplish a complete ureterectomy of the ureter going to the lower half of the left kidney The uppermost calyx from the lower pole ran up into the upper pole for almost an inch This was dissected out without entering the upper pole pelvis The upper three-eighths of the kidney was normal, with apparently a normal ureter The lower five-eighths of the kidney had a thin, mushy cortex There were two sets of vessels The ureter to the lower pole was dilated to within an inch of the bladder Lower down, the two ureters were found to be contained in the same sheath and were difficult to separate It was believed that some injury was done to the normal ureter during the separation, as, following the operation, there was leakage from both wounds for a time The lumbar wound ceased discharging in six days A catheter was passed to the upper pole of the kidney Instillation of colored hippuran into this pelvis refluxed through the ureterotomy wound The catheter was left indwelling for a short time and then removed The leakage ceased and the patient was discharged from the hospital well

Follow-Up—Four months later, an excretory urogram was made, which showed a well functioning residual upper pelvis (Fig 9) Sixteen months later, at cystoscopy, good indigo carmine and clear urine were obtained from the remaining renal segment

Case 12—A G, male, age 40 *Diagnosis* (1) Complete duplication of left kidney and ureter (2) Infected hydronephrosis, lower half left kidney (3) Hydronephrotic, contracted upper left kidney *Operation* Heminephrectomy, left upper pole *Result* Well

For 12 years previous to admission, this patient had had attacks of left loin pain, associated with pyuria At cystoscopy, a large intruding prostate was found, which made catheterization of the ureters difficult The right ureteral orifice was normal, and there was good kidney function on this side On the left side, two ureteral orifices were found One of these was catheterized and an obstruction was met at the 9 cm level This was readily overcome and the catheter passed up into the kidney Twenty-five cubic centimeters of turbid urine, containing a fair amount of indigo carmine, were obtained A pyelogram made through this catheter showed dilatation of the calices in the lower pole of a double kidney

Operation—January 15, 1935 Heminephrectomy, left upper pole (E Beer) The upper pole of the left kidney was found to be collapsed and led into a separate thickened ureter The lower two-thirds of the kidney parenchyma felt normal The upper pole was resected The cut parenchyma was sewn over with underpinned chromic sutures The exact nature of the obstruction of this portion of kidney could not be established It may have been caused by some abnormal vessel, which had not been identified during the operation The patient was discharged from the hospital fully recovered

Follow-Up—Thirty-two months later the patient was still well and had no complaints It has not been possible to get the patient to return recently for check-up on the function of the remaining lower pole

Case 13—C W, female, age 15 *Diagnosis* Complete duplication of left kidney and ureter with ectopic ureter opening just below urethral meatus *Operation* Heminephrectomy, upper pole left kidney, partial ureterectomy *Result* Well

The patient gave a history of constant dribbling of urine since childhood No other urinary symptoms, except frequency The rest of the past history was irrelevant Abdominal examination was negative Just below the urethral meatus in the midline was found a small, teat-like prominence with a tiny opening in it A small ureteral catheter could be passed into this orifice for only 2 cm The urine which dripped from the opening was clear The vagina and vulva were reddened Rectal examination was

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negative Roentgenologic examination showed no spina bifida. At cystoscopy, the bladder and both ureteral orifices were found to be normal. Both ureters were catheterized without obstruction. Clear urine was obtained from both kidneys. The bladder was filled with blue stained solution and a cotton pad placed in the vagina, which became wet, but was not stained blue. This finding ruled out the possibility of a vesicovaginal fistula. The opening below the urethral meatus was then injected with 20 cc of sodium iodide. This was found on roentgenologic examination to have filled the upper pole of a double left kidney. The lower pole was filled by means of a catheter in the left ureteral opening in the bladder (Figs 10A and B).

Operation—September 14, 1928. Left heminephrectomy, upper pole (A. Hyman). The left kidney was exposed and found to be about normal in size. There was a double pelvis, the upper one being markedly hydronephrotic. The upper pole of the kidney was



FIG 10—Case 13 (C. W.) (A) Retrograde ureteropyelogram showing an ectopic ureter on the left side opening just below urethral meatus. Double pyelogram showing normal lower pole with ectopic ureter running toward upper pole. (B) Retrograde ureterogram, filling only the ectopic ureter, showing marked dilatation (ref. A).

resected, as well as the ureter entering the upper pelvis, down to within three inches of the bladder. The postoperative course was uneventful.

Follow-Up—When seen two months later, the patient had no further dribbling. Cystoscopy revealed strong indigo carmine efflux from both ureteral orifices. Eight months later, the patient had no symptoms.

Case 14—S. S., female, age 32. *Diagnosis* (1) Right double kidney with ectopic ureter. (2) Pyonephrosis, left upper pole. *Operation* Heminephrectomy, left upper pole. *Result* Well.

The patient was admitted to the Gynecologic Service two months previously, because of urinary incontinence and frequency which had followed childbirth eight years previously. She had had marked frequency of urination during cold weather since childhood. Anterior and posterior colporrhaphy and parametrial fixation were performed. On the

fifth postoperative day her temperature rose to 103.6° F. On the eighth day, she began to complain of right loin pain. The urine contained a great deal of pus. A tender mass was palpable in the region of the right kidney. This mass rapidly increased in size. Excretory urography revealed a normal, low lying pelvis of the right kidney (Fig 11A) with a large mass to the right of the spine, obscuring the psoas margin. A diagnosis of a retroperitoneal abscess was made.

First Operation—November 12, 1937. Incision and drainage (Dr. A. Hyman). A large encapsulated mass was found. It was opened, and a great deal of thick pus was evacuated. The nature of the mass could not be determined by inspection alone, and a section of the membrane wall was taken for microscopic examination. The pathologic report was "fragment of atrophic kidney tissue with pelvic mucosa, probably a portion of an hydronephrotic sac."

Postoperative Course—Following this procedure the patient's temperature dropped to normal and remained so. The discharge from the wound became minimal, and there remained only a small fistulous tract, which was kept open for further investigation. Indigo carmine, administered intravenously, was not discharged through the fistulous opening. Blue stained hippuran was instilled through the tract, causing the patient to have a desire to urinate after two ounces had been instilled. She was then catheterized and an ounce of unstained, clear urine was obtained. Obviously, therefore, there was no connection between the cavity above and the bladder. Cystoscopy was performed. A single right ureter was catheterized for a few inches with a Garceau catheter (Fig 11B). With hippuran instilled into the fistulous tract at the same time as the Garceau catheter was injected, a simultaneous roentgenogram was obtained (Fig 11C) which showed that we were dealing with a double kidney and double ureter, and that the drainage operation previously performed had drained a pyonephrosis of the upper pole. Both pelvises were dilated. The ureters were tortuous and swung to the right in their mid-portions. The ultimate termination of the ureter going to the upper pole could not be identified (only a single right and left ureteral orifice were seen at cystoscopy). The patient was discharged with the fistulous opening. She returned one month later, having gained ten pounds during the interim, and with the history that she was having attacks of right loin pain. Cystoscopic check-up again revealed only a single right and left ureteral opening. Pyelographic studies corroborated the findings obtained previously. Inspection of the external genitalia and genito-urinary tract did not reveal an ectopic ureteral opening after instillation of blue-stained solution into the upper pole of the kidney through the fistulous tract. However, pressure over the right vaginal wall caused a reflux spurting of the blue solution through the fistula. It was then fairly obvious that we were dealing with an instance of double kidney with an ectopic, right ureteral implantation, although the ureter opening was not seen.

Second Operation—January 4, 1938. Heminephrectomy, right upper pole, and partial ureterectomy down to the iliac vessels (E. Beer). The kidney was exposed. The ureters were adherent to the anterior portion of the previous wound. One ureter was 2 cm in diameter and very much thickened. The other was slightly larger than normal, soft and healthy looking. After identifying the two ureters, they were followed up toward the kidney and the normal appearing one was found to enter the lower two-thirds of the kidney, whereas, the thick ureter entered the upper pole. The upper pole was separated from the lower pole, using one finger in the upper pyonephrotic sac as guide for the line of separation. The vascular supply to the lower part of the kidney was left intact, very little vascular pedicle was identified, going to the atrophic and pyonephrotic upper pole. Following the separation of the upper pole, the bleeding from the cut kidney surface was controlled by three or four underpinned chromic sutures. The large ureter was then dissected free, down to the iliac vessels, and carefully separated from the other ureter, which was contained in the same sheath. The diseased ureter was tied at the level of the iliac vessels and divided with a carbolyzed knife. It was not



FIG 11—Case 14 (S S) (A) Excretory urogram showing lower pole of double kidney, no excretory media from upper pole (ref B and C) (B) Retrograde pyelogram showing outline of lower pole of duplicated right kidney (ref A and C)

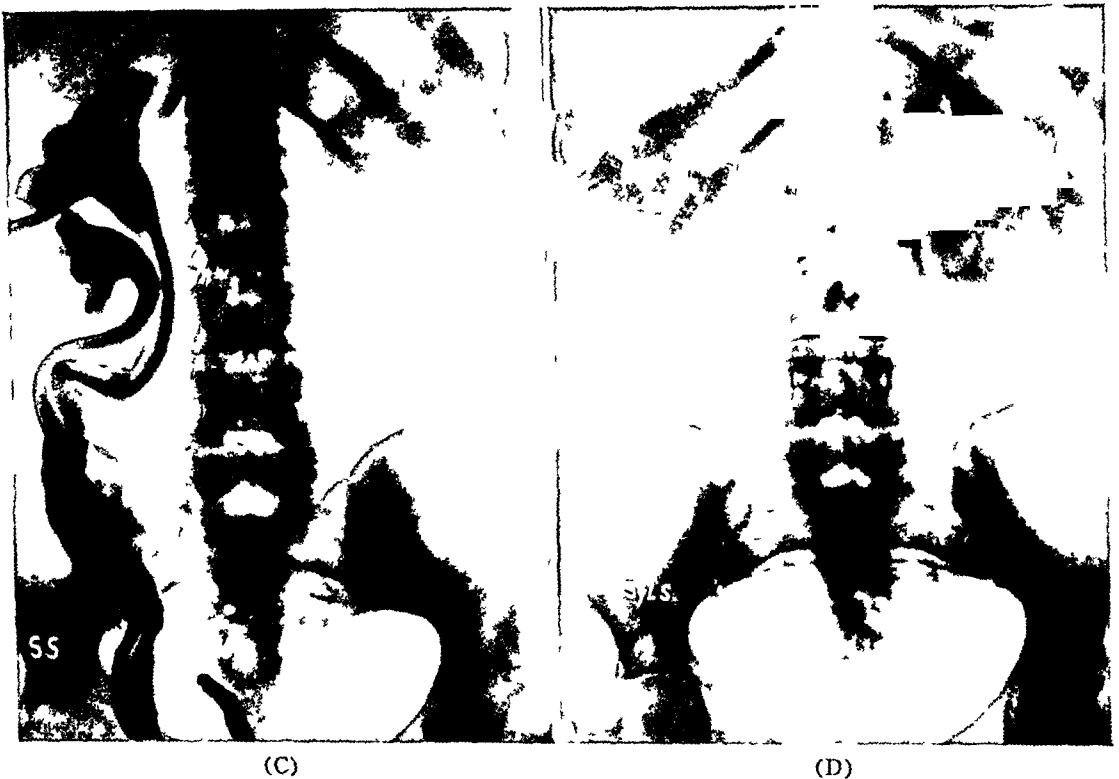


FIG 11—(C) Roentgenogram taken after simultaneous instillation of radiopaque solution through the nephrostomy tube and through the ureteral catheter, showing double kidneys (right) and ureters. Note the dilatation of the upper pelvis and its ureter which was found to end blindly in the right anterior vaginal wall. (D) Excretory urogram four months postoperatively showing good function of the conserved upper two-thirds of the right kidney. Right ureter can be seen as in the original pictures, displaced far from the spine.

TABLE VI
SYNOPSIS OF 14 CASES OF HEMINEPHRECTOMY, OPERATED UPON FOR DISEASE OF A DOUBLE KIDNEY

Case No	Sex	Age	Anomaly	Pathology	Operation	Pole Involved	Follow-Up on Remaining Pole
1 L A	F	29	Right double pelvis and ureter, complete duplication	Pyonephrosis, right lower half	Right heminephrectomy, complete ureterectomy	Lower	3½ years, good function
2 A T	M	40	Right double pelvis, partial duplication of ureter	Dendritic stone, right lower pole Hydronephrosis, both right pelvis Left hydronephrosis	Right pyelolithotomy, lower pole nephrostomy, heminephrectomy, lower pole	Lower	Leakage from wound
3 D A	F	40	Right double pelvis, partial duplication of ureter	Pyonephrosis, right lower pole	Right heminephrectomy, ureterectomy, to 1 inch from bladder	Lower	No follow-up
4 L G	M	44	Horseshoe kidney, complete duplication left kidney and ureter	Hydronephrosis, left upper pole Pyonephrosis, left lower pole	Heminephrectomy, lower half left horseshoe kidney Ureteral anastomosis (ureter going to upper pole inadvertently injured)	Lower	Some urine from upper pole 1 month later, no further follow-up
5 N R	M	44	Left double pelvis, partial duplication of ureter	Calculus hydronephrosis, left upper pole	Heminephrectomy, left upper pole	Upper	7 years, excretory urogram, good function
6 L F	F	42	Complete duplication left kidney and ureter	Nephrolithiasis, left lower pole	Heminephrectomy, left lower pole	Lower	Died 3 hours postoperatively, shock
7 M W	M	30	Complete duplication left kidney and ureter	Pyonephrosis, left lower pole (aberrant vessel), perinephritis	Heminephrectomy, left lower pole	Lower	7 years, excretory urogram, good function

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8	S S	M	47	Complete duplication right kidney and ureter	Calculus, lower pole right kidney	Heminephrectomy, right lower pole	Lower	5 years, excretory uro- gram, good function
9	M O	M	23	Bilateral, complete du- plication kidneys and ureters	Hydronephrosis, right upper pole Atrophy, right kidney Hydrone- phrosis, left lower pole with hydro-ureter	Right nephro-uretereec- tomy (complete) Hemi- nephrectomy, left lower pole	Lower	11 years postoperatively, patient still living, good function
10	J G	F	10	Bilateral, complete du- plication kidneys and ureters	Pyonephrosis, left lower pole	Heminephrectomy, left lower pole	Lower	8 months postoperatively, good function
11	R W	F	8	Complete duplication left kidney and ureter	Pyonephrosis, left lower pole	Heminephrectomy, left lower pole, complete ureterectomy	Lower	1 1/2 years postoperatively, good function
12	A G	M	40	Complete duplication left kidney and ureter	Infected hydronephro- sis, left lower pole Hy- dronephrotic contracted, left upper pole	Heminephrectomy, left upper pole	Upper	2 years postoperatively, no symptoms
13	C W	F	15	Complete duplication left kidney and ureter Ectopic left ureter (urethra)	Ectopic ureter going to upper pole	Heminephrectomy, left upper pole	Upper	2 months postoperatively, strong indigo carmine both kidneys 3 years later no complaints
14	S S	F	32	Right double kidney (ureter to upper pole ap- parently ending blindly in anterior vaginal wall)	Pyonephrosis, right up- per pole	Heminephrectomy, right upper pole	Upper	4 months postoperatively, excretory urogram, good function

considered advisable to remove the entire ureter, since this procedure would have entailed making a second incision in the abdominal wall, with certain resultant contamination from the loin wound. It was appreciated that fluid might collect in the remaining portion of the ectopic ureter and that it would probably present itself as a cystic dilatation in the right anterior vaginal wall, which could be dealt with subsequently by a simple incision.

Subsequent Course—This cystic dilatation, corresponding with the lower stump of ureter, did occur in the vaginal wall, associated with fever. Incision and drainage was performed and pus was evacuated. The cavity was kept open for a number of days, and the patient discharged for further dressings in the dispensary. Four months postoperatively, an excretory urogram showed good function of the remaining lower pole (Fig 11D).

Recapitulation of the Present Series of 14 Cases—In our experience with 14 cases of heminephrectomy, there was a single operative mortality (Case 6), or 7 per cent. The disease was limited to the upper pole in four cases (28 per cent), and of these four cases, two had ectopic ureters. The upper pole and its ureter were removed, preserving for the patient the lower half of the kidney. In ten cases, the lower pole showed involvement, and in these the lower half was removed, allowing the upper portion to remain. The nature of the lesion in six cases was pyonephrosis, in five cases it was hydro-nephrosis, one case had a calculous hydronephrosis, in two cases there were multiple calculi. In none of our cases was it necessary to perform a secondary nephrectomy of the residual portion.

Stone¹² calculated that in a series of 30 collected cases, 10 per cent required secondary nephrectomy. It is also of interest to note that in 12 of the 42 nephrectomies reviewed by Eisendialth,³¹ there was no abnormality in one segment, in other words, heminephrectomy would have been the more conservative procedure. In five additional cases in his series, technical difficulties prevented a planned heminephrectomy, and a complete nephrectomy was performed.

In those cases which we have been able to follow up by cystoscopy or pyelography, all of them showed good function of the remaining portion of kidney at variable lengths of time after the operation.

It is evident, therefore, from a study of these cases that conservatism is most important, and that kidney tissue should be saved whenever possible. This point may be emphasized by reference to Case 9, who has been living for 11 years on what amounts to approximately one-sixth of the normal amount of kidney parenchyma.

SUMMARY AND CONCLUSIONS

(1) A series of 104 cases of double kidney is presented and an analysis of these cases emphasizes the well known statement that an anomalous kidney is prone to disease.

(2) Sixty per cent of these cases had symptoms, and 25 per cent required some operative procedure.

(3) Fourteen of these cases required a heminephrectomy, which is discussed from the standpoint of indications, contraindications and technic.

(4) The conclusion is reached, after follow-up study of these 14 cases,

that conservation of renal tissue is indicated in instances of double kidney and that heminephrectomy fulfils this purpose. Of the 14 cases of heminephrectomy, ten were adequately controlled by cystoscopy, excretory urography or both, the residual part of the kidney was found to function satisfactorily.

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DENERVATION OF THE BLADDER FOR RELIEF OF INTRACTABLE PAIN

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INTRACTABLE bladder pain associated with frequency and tenesmus is always a very distressing condition. When, however, it continues steadily for months at a time, it may completely undermine both the morale and the recuperative powers of the patient. There are two chronic diseases, namely, tuberculosis of the bladder and interstitial cystitis, in which this distressing syndrome is particularly apt to occur in a form which fails to respond to the usual methods of conservative treatment. Tuberculous cystitis is nearly always secondary to tuberculosis of the kidney. Consequently when the major infection is limited to one kidney, its removal generally allows the tuberculous involvement of the bladder to clear up. When both kidneys are involved in open lesions, however, there is a continuous and inevitable reinfection of the bladder, which frequently makes ineffective all measures directed toward the alleviation of symptoms from the local tuberculous ulceration. The effect of the pain and loss of sleep in patients combating a tuberculous involvement is distinctly harmful. In interstitial cystitis also, although many cases respond favorably to conservative measures, there are others in which the whole gamut of such procedures leaves the agonizing symptoms unaffected. Thus one of the cases which we saw had been treated energetically for a year by a very competent urologist who used all of the methods usually employed. Yet, in spite of this conscientious treatment, the patient was in constant pain, voiding every ten or 15 minutes, day and night, haggard from the loss of sleep, his morale completely shattered and having sustained a weight loss of 25 pounds. His actual survival depended upon obtaining relief.

Confronted with such examples of intractable vesical pain, it is quite comprehensible that numerous attempts have been made to produce an effective sensory denervation of the bladder. The great obstacle in the way of the successful accomplishment of this aim has been the threefold pathway of afferent impulses from the bladder—namely, the pelvic nerves (parasympathetic), the hypogastric nerves (sympathetic) and the internal pudendal nerves (somatic). Although all three of these routes probably do carry painful sensation from the bladder, and would all have to be interrupted in order to produce a complete sensory denervation of the bladder, they are not of equal clinical importance in the relief of intractable pain, nor, fortunately, is it necessary to interrupt them completely in order to alleviate the distressing symptoms.

Among the early attempts to control intractable bladder pain, the most drastic was the extirpation of the hypogastric ganglion. This procedure, of

course, produced a total paralysis of the emptying power of the bladder and consequently was quickly abandoned. The relief of other forms of pelvic pain, particularly those associated with the uterus, had been attempted with a considerable degree of success by the Lyonnais surgeons, Leiche and Cotte, and the technic of such sympathetic denervation by excision of the superior hypogastric ganglion has been fairly well standardized. The Italian surgeon, Pieri,¹ was the first to successfully carry out this procedure for the relief of bladder pain in two cases of tuberculous cystitis. Since that time, there have been scattered reports of individual cases or small groups of cases treated in this manner. Leimonth and Braasch² assembled 12 cases of vesical pain treated by sympathetic neurectomy. Only one of these cases was due to tuberculosis. Douglass³ reported five cases of interstitial cystitis treated in this manner. The most striking thing in regard to the results, in the few scattered cases recorded in the literature, is the marked variability in the degree of relief afforded the various patients. Thus one would obtain almost complete relief from excruciating pain while in another it would continue largely unabated. Leimonth⁴ stated that he had not yet been able to recognize the factors that made for success in some cases and failure in others.

Another idea suggested in the literature was that the improvement obtained in the favorable cases lasted only a few months and was not permanent. There were no data in the cases reported concerning any results later than a few months after operation. It was to gain further knowledge on these two important points that the present study was undertaken. Our series includes 11 patients with intractable bladder pain which we have sought to relieve by partial denervation of the bladder. Eight of these patients had tuberculous cystitis and three had interstitial cystitis.

The extreme variation that is found in the topographic anatomy of the sympathetic nervous system is generally appreciated. Therefore, the first point to be considered was that such a variation accounted for the lack of uniformity in the results obtained. Or, in other words, that the unsuccessful cases did not have complete interruption of the sympathetic pathways. When the operation is carried out by the standardized technic for the resection of the superior hypogastric plexus (Cotte's operation), there were two particular sources of error which we had learned from our previous experience in attempting to control other types of pelvic pain. In some cases fibers extend from the inferior mesenteric plexus to one of the separate hypogastric nerves, especially the left one, well below the bifurcation of the plexus. These are interrupted only by lifting up and freeing the posterior surface of the inferior mesenteric artery and its continuation as the superior hemorrhoidal artery deeply into the pelvis, and dividing all fibers extending backward and downward from it. Another set of fibers was found fairly frequently which escaped division by the Cotte type of operation. These were sympathetic nerve fibers from the hypogastric ganglion or lower parts of the hypogastric nerves running upward and laterally directly to the sacral sympathetic chain on one side or the other which they then joined. Douglass

has also observed such branches going directly to the pelvic sympathetic chain and PIERI in his second paper advised ramisection of this chain presumably in order to interrupt such pathways

As our first procedure, then, we extended the sympathetic interruption to include not only excision of the superior hypogastric plexus but also those fibers from the distal part of the inferior mesenteric and superior hemorrhoidal artery, and also those fibers going directly to the sacral chain. We accomplished the latter, not by attempting the hopeless task of dissecting out the individual fibers retroperitoneally very deep in the pelvis, but by removing the upper part of the sacral sympathetic chain including the first and second sacral ganglia. (The dissection must not be carried so deeply that

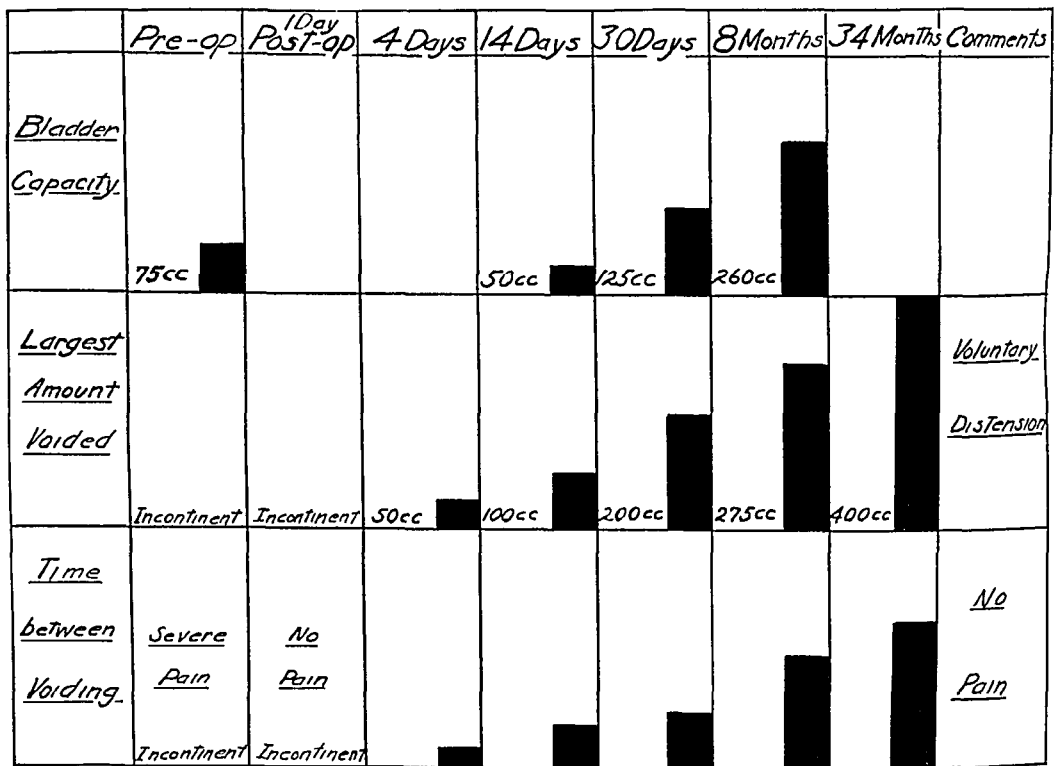


CHART I—Case 3 Showing, graphically, the result of sympathetic denervation in tuberculous cystitis

the sacral [parasympathetic] nerves are injured.) In our second case, a young man, with bilateral renal tuberculosis and tuberculous cystitis, the left sacral chain was not disturbed for technical reasons. We found that this patient had much more pain than the succeeding ones on distention of the bladder after operation. Consequently, in subsequent cases we have been careful wherever possible to remove the upper sacral chain.

In the eight cases of tuberculous cystitis, sympathetic denervation has resulted in a marked decrease in the amount of pain suffered, often with an increase in bladder capacity and a decrease in the frequency of voiding. Case 3 illustrates the marked improvement obtained (Chart I). This patient had been suffering so severely from pain and frequency that she had been

on constant catheter drainage for eight months. Her bladder capacity was approximately 100 cc. Within four days after operation, her pain and frequency had markedly diminished. Her bladder capacity gradually increased, aided by dilatation, to 350 or 400 cc and now three years after operation, she is having practically no bladder pain. The other cases of tuberculous cystitis have also shown a marked relief from pain. On the other hand, the cases of interstitial cystitis have shown a much more varied type of response. One patient showed a most striking relief of pain, one a moderate relief and one very little improvement.

We concluded, therefore, that in tuberculous cystitis, sympathetic denervation of the bladder could be relied upon to relieve the pain to a marked extent with a variable increase in bladder capacity, while in interstitial cystitis, the result was much more uncertain.

This difference in the results achieved by sympathetic denervation in tuberculous and interstitial cystitis could not be explained on the basis of individual variation in the nervous pathways. The only explanation that seemed reasonable for this discrepancy was in the site of the bladder involvement. In tuberculous cystitis, the chief area of irritation is in the trigonal region, whereas, in interstitial cystitis, it was more apt to be in the fundus of the bladder. Just how sympathetic denervation acts to relieve the bladder pain is uncertain, but as Learmonth⁵ and Cheetham⁶ reported, there is regularly a diminished tonicity in the trigonal region and a relaxation of the internal sphincter following sympathetic denervation. The mechanism of the production of visceral pain is not finally settled, but in the bladder as in other viscera, as Learmonth⁷ states, the majority of observers are agreed that pain arises as the result of tension in the viscus, whether from distention, from inability to evacuate its contents, or from incoordination of the muscular contraction. Consequently in the cases relieved of pain following sympathetic denervation, it is uncertain whether the relief is due to actual interruption of afferent pathways over which pain is carried or whether this result is due to the relaxation of the trigone and internal sphincter, the contraction or spasm of which would otherwise cause pain. This hypothesis would also explain the marked variability which other observers have found, as well as ourselves, in the relief of pain by sympathetic denervation in interstitial cystitis. If the area of irritation of the bladder wall was in the region of the trigone, then sympathetic denervation would be likely to afford a major degree of relief, whereas, if the focus of irritation were chiefly in the fundus, it would not.

In order to increase the bladder capacity in these patients, it is often desirable to carry out a progressive dilatation of the bladder for several weeks or months after operation. We are convinced that the discomfort associated with such forceful dilatation is more effectively abolished by this more complete form of sympathetic denervation which we have carried out than by the simple removal of the superior hypogastric plexus alone. We have also established the fact that the relief of pain achieved by sympathetic denerva-

tion is not merely a temporary effect. We have observed, in our cases, that it continues for at least three years.

One further step has been added in the effort to produce more complete relief. This arose in connection with Case 6. For technical reasons due to a previous inflammatory episode, it was thought inadvisable to attempt exposure and removal of the right upper sacral chain. Although this patient had experienced some relief of pain after operation, it was quite incomplete. Subarachnoid alcohol injection was then employed, and was found to be very successful in relieving the residual pain. Consequently, this additional step is now used when the patient has persistent pain after sympathetic denervation. Possibly in those cases where the trigonal region is not involved, certain cases of interstitial cystitis, intraspinal alcohol alone would suffice to relieve the patient. This question should be further investigated. Where the trigonal region is chiefly involved, probably sympathetic denervation will be found irreplaceable and the intrathecal injection of alcohol only a subsidiary method. Unusual precautions should be taken in administering the alcohol injections to prevent any injury to the motor nerves of the bladder. This phase is being presented in a subsequent communication.⁸ The subarachnoid injection of alcohol, as used in these cases, probably actually interrupts, in the intraspinal part of the posterior roots, some, at least, of the fibers from the pelvic and internal pudendal nerves carrying the painful impulses from the bladder to the cord.

There is one further step in the clinical investigation of these cases of intractable bladder pain that we are now investigating, namely the results obtained by temporarily interrupting the sympathetic nerves and the pelvic roots separately. Flothow⁹ has suggested and described a relatively simple method for anesthetization of the hypogastric nerves. A low spinal anesthesia, on the other hand, will block the sacral nerves while sympathetic pathways which reach the spinal cord at a much higher level will be intact. By studying the effect on the pain of these two procedures as a preoperative test, it is our belief that, in the future, we can intelligently select the type or types of denervation that will relieve the intractable pain of tuberculosis of the bladder and interstitial cystitis.

CASE REPORTS

Case 1—No 90961. M. D., female, age 12. C. C. Frequency of urination. P. I. Six years ago, patient first noted intermittent attacks of frequency of urination and dysuria. Four years ago, acid-fast bacilli were identified in the urine from each kidney. Frequency gradually increased to every half hour and incontinence at night. Treated at sanatorium four years. Unable to attend school. P. H. Scarlet fever at age 8, without complications. F. H. No tuberculosis or known contacts.

P. E. Undernourished girl, age 12 appearing chronically ill. Teeth. Two carious. Tonsils large and cryptic. Neck. Small, shotty nodes. Lungs. Clear to auscultation and percussion. Heart. Soft systolic murmur at apex. B. P. 148/80. Abd. No masses or tenderness and no C. V.-angle tenderness posteriorly. Lab. Urine. Alb. 1 plus, 1-2 W. B. C. per H. P. F., no R. B. C., acid-fast stain negative. Guinea-pig positive for tuber-

culosis P S P, 35 per cent first half hour, 60 per cent in two hours Urea clearance First hour C M 85 per cent, second hour C M 79 per cent

Cystoscopic examination, under caudal anesthesia, with bilateral pyelograms Showed bilateral calcium deposits in both kidney regions with deformity of calcine structure Indicative of bilateral renal tuberculosis Bladder capacity 80 cc Frequency every half hour

Operation—July 3, 1934 A superior hypogastric plexectomy and excision of the sympathetic chain from the first to third sacral ganglion was performed

Postoperative Course—Wound healed by primary intention On the tenth P O day, bladder capacity 150 cc and frequency reduced from every 15 to 30 minutes to one to one and one-quarter hours Followed in outpatient department by weekly bladder dilatation and gomenol instillations After 12 weeks, was able to attend school for the first time in four years No enuresis Able to go two hours between voidings Five months after the operation, frequency of every two hours, bladder capacity 180 cc, no pain whatsoever

Case 2—No 69243 A F, male, age 26 C C Frequency and dysuria P I Three years before admission began to notice increasing dysuria, frequency and nocturia every one-half to one hour Associated with suprapubic discomfort and cloudy urine P II Noncontributory F H Negative for tuberculosis or contacts

P E Young adult male, undernourished and appearing chronically ill Neck No enlarged nodes or scars Lungs Negative to auscultation and percussion Abd No C V-angle or kidney tenderness anterior Tender over suprapubic area Genitalia Epididymis and vasa normal Rectal Prostate indurated in both lateral lobes, also seminal vesicles Lab Blood studies not abnormal Wassermann negative N P N, 35 Urine Alb 1 plus, acid, cloudy, many W B C and acid-fast bacilli P S P, 77 per cent in two hours

Intravenous pyelography showed a destructive lesion in both kidneys At cystoscopy the left ureter only could be catheterized Positive for acid-fast bacilli Guinea-pig inoculation was positive Discharged to sanatorium for treatment *Diagnosis* Bilateral tuberculosis of the kidneys

The patient was readmitted to the hospital in October, 1934, two years later, at which time the bladder capacity was 90 cc, frequency every half hour, accompanied by severe, burning dysuria Had lost weight and strength and was going down hill Cystoscopic examination showed the bladder to be markedly inflamed, with golf hole ureteral orifices on both sides No attempt made to catheterize the ureters

Operation—October 5, 1934 Resection of the superior hypogastric plexus and excision of the right sacral sympathetic chain from the first to third sacral ganglion was performed

Postoperative Course—Relief of pain on voiding and suprapubic discomfort Bladder capacity raised to 175 cc voluntarily Patient was given bladder dilatation and instillations Further dilatation than 155 cc with irrigator caused severe renal colic on right side (Dilatations similar to those employed by Bumpus in treatment of interstitial cystitis, i.e. with irrigator four feet above patient, giving approximately 120 Mm mercury hydrostatic pressure)

Eight months after operation, goes as long as two hours between voidings Nocturia four times No bladder or suprapubic discomfort Occasionally slight terminal dysuria referred to urethra Has gained in weight and strength, able to work as apprentice printer

Case 3—No 81804 I C female, age 18 C C Frequent and painful urination P I Fifteen months before admission, patient began to notice painful frequent urination which gradually increased up to incontinence, especially at night Three months after onset noted radiating pain from right C V-angle to groin Was cystoscoped at another hospital and a diagnosis of bilateral tuberculosis of the kidneys was made confirmed by guinea-pig inoculation and the patient was sent to a sanatorium for treatment, where

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frequency increased to every 15 minutes Placed on constant catheter drainage for eight months PH Six years previously, loss of weight and strength, no diagnosis made Four years ago pain in right shoulder, which later became ankylosed, without drainage FH No tuberculosis or contacts

PE Undernourished girl, age 18, appearing to be in continual distress from bladder pain Right shoulder ankylosed at the humeroscapular joint Lungs Right apex fine crepitant rales Abd Scaphoid, right kidney lower pole tender on palpation Right CV-angle tenderness Lab RBC 4,900,000, WBC 12,000, Hb 90 per cent, PSP, 35 per cent in two hours Urine Alb and sugar negative, rare WBC and RBC, many bacilli (gram-negative) Acid-fast bacilli present Guinea-pig positive Wassermann negative

When first seen, the patient was leading a catheter life Bladder capacity could be raised to 75 cc, which, however, caused severe pain to develop in the right CV-angle, accompanied by chills and fever following each bladder dilatation attempted

Operation—November 13, 1934 Resection of superior hypogastric plexus and exeresis of the sympathetic chain, bilaterally, from the first to the third sacral ganglion, was performed

Postoperative Course—Incontinent for first three days, but had complete relief from pain In six days, was voiding every three-quarters to one hour In one month, bladder capacity 125 cc and patient going up to two hours between voidings Nocturia four times In two and one-half months, bladder capacity was 290 cc and continues between 275 to 300 cc since (Chart 1)

Case 4—No 12743 R B, male, age 42 CC Painful frequent urination PI Seven years before admission, patient first noted nocturia followed by hematuria Two months later, swollen left epididymis, which broke down, drained and healed slowly Following this he developed severe dysuria and frequency Right epididymitis developed two months before admission, with epididymectomy elsewhere Symptoms increased, so that he was voiding every ten to 15 minutes, day and night, with severe dysuria No relief by bladder irrigations and instillations PH 1911, pleurisy with effusion 1912, tuberculosis right hip with draining sinuses and ankylosis 1927, Pott's disease with psoas abscess 1928, ischiorectal abscess, left tuberculous epididymitis 1930, tuberculosis left hip with ankylosis

PE Undernourished male, age 42, appearing chronically ill Both hips were ankylosed in an extended position In continual distress from pain and frequent urination Numerous scars and draining sinuses over hips, genitalia and lower extremities Teeth Carious Lungs Negative on repeated examinations BP 118/62 Heart Normal Abd Tip of spleen felt No CV-angle tenderness Moderately severe suprapubic tenderness Genitalia Draining sinuses from epididymies Vasa indurated and nodular Rectal Prostate firm and irregular Lab Urine Alb 2 plus, 15-20 WBC per HPF, no RBC Guinea-pig positive for tuberculosis NPN 40, RBC 3,500,000, WBC 12,350 Cystoscopy enabled one to see only vault of bladder because of ankylosis of hips and spine Intravenous pyelograms showed evidence of a destructive lesion in both kidneys

Operation—November 21, 1934 Resection of the superior hypogastric plexus and exeresis of the sacral sympathetic chain from the first to the third ganglion was performed

Postoperative Course—Continued to void frequently for two days, but had no pain Seven days postoperative, wound broke down, requiring secondary closure In three weeks, patient was going as long as two and one-half hours between voidings with no dysuria, bladder capacity 175 cc At eight months, he was voiding every two and one-half to three hours, without pain He has had no dilatations or bladder treatments since operation

Case 5—Hosp No 77573 A B, male, age 48 CC Frequent painful urination PI Began four years before admission with gradually increasing frequency of urina-

INTRACTABLE BLADDER PAIN

tion and dysuria, especially terminal Ten months before admission, had frank hematuria, and following this, became symptomatically much worse Voided as frequently as every three to ten minutes, day and night, with severe pain, and developed bilateral tuberculous epididymitis Treated at a Veterans' Hospital for three months with usual measures without relief Then treated in the outpatient department with bladder irrigations with various drugs, bladder dilatations and bladder instillations of gomenol, following which he voided less frequently, but pain continued P H Twenty years ago, had pleurisy with effusion Nine years ago, had frank hemoptysis, treated with sanatorium regimen and tuberculosis apparently arrested

P E Undernourished white male Teeth In poor state of repair Voice Slightly husky Lungs Dulness in both apices with fine râles in right apex, both anterior and posterior Abd Neither kidney felt or tender Suprapubic tenderness Rectal Tone good Bilateral indurated epididymis both very sensitive Prostate slightly enlarged, firm and irregular with induration of seminal vesicles, suggesting bilateral tuberculous seminal vesiculitis and prostatitis Lab Acid-fast bacilli from both kidneys Typical tuberculous lesions found in microscopic sections from removed epididymies At cystoscopy, under caudal anesthesia, the bladder capacity was raised to 125 cc Bilateral pyelograms (retrograde) showed deformities typical of tuberculosis, which was confirmed by guinea-pig inoculation

Operation—March 23, 1935 Presacral neurectomy and exeresis of both sacral sympathetic chains including one to two sacral ganglia was performed

Postoperative Course—During the first few days, voided small amounts frequently, then capacity rose to 275 cc on third postoperative day, and went two to three hours between voidings, which improvement has continued Patient has no pain or dysuria In the outpatient department he is continuing with bladder dilatations and instillations at regular intervals to keep his bladder capacity up

Case 6—No 2178 J A G, female, age 26 CC Painful frequent urination P I First seen in February, 1934 Six months previously began to notice frequency every hour and nocturia every two hours Voided about 60 cc at a time There was associated pain in the right groin which radiated to the urethral meatus Marked dysuria has been present since onset F H Three relatives died with tuberculosis No known contacts *Diagnosis* Tuberculosis in the right kidney A nephrectomy and ureterectomy was performed in March, 1934 Frequency persisted in spite of the nephrectomy, and general and local measures toward treatment of the cystitis A hysterectomy was performed in January, 1935, for fibroid uterus Bladder symptoms persisted, the patient was voiding every five to 15 minutes with considerable pain

Operation—December 2, 1935 Presacral neurectomy and a unilateral (left) exeresis of the sacral sympathetic chain was performed It was impossible to attack the right ganglia because of adhesions of the peritoneum and stump of the uterus

Postoperative Course—Within six days, frequency was diminished to every two to three hours, and within 13 days the bladder capacity could be raised to 300 cc, although some pain persisted and there were periods in which the frequency would recur Subarachnoid alcohol was undertaken with the patient lying on her left side, in April, 1936, using 0.75 cc of absolute alcohol This was repeated with the patient lying on the opposite side, in June, 1936, since which time, she has had complete relief of pain in her bladder, dysuria, and frequency She voids now every three to four hours and nocturia two times (which has persisted up until the present time)

Case 7—No 2906-J R M, female, age 32 CC Painful frequent urination Pain in urethra on walking P I Patient had symptoms of tuberculous cystitis with frequency and dysuria seven years ago Nephrectomy performed, with relief of all bladder symptoms until nine months ago, then noted gradually increasing frequency and nocturia with associated dysuria, and for the last two months noted marked frequency every 15 to 20 minutes and urethral pain on walking P H Also had pulmonary tuberculosis and apparent arrest in process by collapse therapy

P E Young, adult female, appears chronically ill but fairly well nourished Lungs Thickened pleura but no active lesions Abd Scar of nephrectomy on left No palpable organs or masses Right kidney region not tender Pelvic Urethral orifice red and pouting Entire urethra tender on pressure Lab Acid-fast bacilli in urine from remaining kidney Secondary infection with bacilli (many) The patient was treated by all types of irrigation, instillation and mouth medication with symptoms increasing for nine months Cystoscopy revealed urethritis, cystitis with ulcers near both ureteral orifices and right lateral wall of bladder

Operation—September 30, 1937 Presacral neurectomy and exeresis of lateral sacral sympathetic chain from first to third ganglion, bilaterally was performed

Postoperative Course—Relief of pain except in urethra Frequency every 30 to 45 minutes Incontinent for first two days, then occasionally nocturnal enuresis for two weeks Three months later secondary infection became marked, accompanied by severe urethral burning on walking, with frequency at times half hourly, but could go up to two hours while at rest Intrathecal alcohol injection, February 8, 1938, with right side uppermost, almost entire relief of pain with frequency diminished to three hours February 14, 1938, intrathecal alcohol injection with left side uppermost Complete relief of pain Frequency every three to four hours, day and night Walks without pain in urethra

Case 8—Hosp No 25163 R C, female, age 44, was originally admitted to Iola Tuberculosis Sanatorium, in 1929, for minimal pulmonary tuberculosis In 1933, she had tuberculosis of the left hip for which she was twice fused, in 1933, and again in 1934 She was readmitted to Iola Sanatorium in January, 1937, for reactivation of pulmonary tuberculosis, and shortly thereafter developed tuberculosis of the left sacro-iliac joint, for which a fusion was performed Shortly thereafter, she developed frequency and burning, hematuria and pyuria Tubercle bacilli were demonstrated in the urine In spite of conservative measures, the bladder pain became increasingly severe, and wearing on the patient, causing her to lose much sleep

Operation—September 9, 1937 The superior hypogastric plexus and the right upper sacral sympathetic chain were excised The left sacral chain was so embedded in scar tissue from the sacro-iliac disease that it was considered inadvisable to attempt its removal The patient was transferred back to Iola Sanatorium on the eleventh post-operative day, markedly relieved of her bladder pain If her symptoms recur (associated with the incompleteness of the operation), it is planned to reinforce the operative treatment with subarachnoid alcohol injection

Case 9—G P, male, young adult This was a patient seen in consultation with Dr Elmer Belt, at the Good Samaritan Hospital, Los Angeles, Calif He had the typical findings of an interstitial cystitis of severe grade In spite of vigorous conservative measures, the bladder pain, tenesmus and frequency continued without relief The patient in the previous six months had lost 25 pounds in weight from the constant pain and loss of sleep He had to void every ten to 15 minutes, day and night Doctor Belt was planning to give him relief by transplanting his ureter into the colon

Operation—The superior hypogastric plexus and the upper sacral sympathetic chains were removed July 7, 1935

Postoperative Course—Six weeks later he had regained 20 pounds in weight, was voiding every three or four hours, his bladder capacity was 300 cc, and his only annoying sensation was a burning in the urethra during urination His bladder pain apparently had been completely eliminated and his general health was excellent This improvement continued until he was lost track of about a year after operation

Case 10—Hosp No 94259 E H, female, age 23 This patient presented a typical example of interstitial cystitis She had been in the hospital on seven previous occasions, during the past three years She had had numerous courses of irrigations, instillations, fulgurations and dilatations of the bladder without any lasting effect on the severe pain, tenesmus, nocturia and frequency Her bladder capacity was 80 to 90 cc and she voided every 15 to 30 minutes Urine culture had shown *Staphylococcus albus*, *B coli*,

B. proteus, *B. aerogenes* and *B. alkaligenes* on various occasions but no tubercle bacilli on guinea-pig inoculation

Operation—The superior hypogastric plexus and the upper sacral sympathetic chain on each side were removed June 5, 1937

Postoperative Course—Within two weeks her bladder capacity had increased to 200 cc and her symptoms were much improved. However, within six months her dysuria and frequency had returned, with a highly infected urine, and it was felt that the sympathetic denervation had not helped her very appreciably

Case 11—Hosp No 131876 E C, male, age 54. For over two years this patient had had frequency, urgency, burning and nocturia. The pain on urination had increased. Various conservative measures had failed to relieve it. Cystoscopy showed numerous bleeding areas along the right and left walls and over the fundus of the bladder. Tubercle bacilli were absent from the urine

Operation—October 20, 1937. The superior hypogastric plexus and both upper sacral sympathetic chains were removed

Postoperative Course—The patient obtained a considerable degree of relief. The frequency and pain were much less, the bladder capacity increased from 100 to 275 cc with the aid of dilatations. At present he still has some bladder pain but much less than before operation, and he now sleeps well at night. We have offered him subarachnoid alcohol injection but he does not feel that the pain is sufficiently troublesome to warrant coming in to the hospital for this at present

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DISCUSSION—DR LOYAL DAVIS (Chicago, Ill.) Mr President and Gentlemen. I think that Doctor Scott's paper and his work offer a very excellent example of the clinical application of known physiologic and anatomic facts in a field which is very difficult to investigate from a purely experimental standpoint through the employment of animal investigation.

We have been interested for a considerable period of time in the pathway of pain impulses, particularly from the viscera, and our chief concern has been to try to work out the mechanism for the pathway of these visceral afferent impulses.

As Doctor Scott has said, he has been unable to give a conclusive answer to the question of whether or not the painful impulses are the result of the action of the efferent mechanism of the sympathetic fibers, which produces

contraction of smooth muscle, in itself is painful, and which are then carried by the ordinary somatic nerves to consciousness, or whether the visceral painful impulses are transmitted by an afferent mechanism over the sympathetic fibers

As he has told you, the innervation of the bladder is an extremely complicated one, and, as he has pointed out, there are various regions of the bladder which are innervated by sympathetic fibers coming from the thoracic lumbar segment of the spinal cord, and other portions of the bladder which are innervated by fibers coming from the sacral portion of the cord, in other words, parasympathetic fibers

Both of these types of fibers contain small myelinated and unmyelinated fibers which could carry afferent impulses. In other words, both the pelvic nerves and the hypogastric nerves to the bladder are both motor and sensory in function. Although Doctor Scott has unquestionably obtained clinical relief in his cases, we are not much nearer to the solution of the exact mechanism resulting in visceral pain, because in removing the hypogastric supply to the bladder, both efferent and afferent fibers have been sectioned.

I think it is in this type of work—the clinical application of known physiologic and anatomic facts—which will finally bring solution of the mechanism of the relief of pain. I feel very strongly that the section of sympathetic fibers for the relief of vesical pain is not as effective as the interruption of the pathway, either within the spinal cord or before the fibers get to the spinal cord in the dorsal roots, because I think the mechanism is an efferent and not an afferent one.

In performing a chordotomy, for the relief of visceral pain, it is necessary to make a deep section within the spinal cord so that a portion of the gray matter of the cord is interrupted, because visceral fibers which carry pain go into the spinal cord and then ascend in the cord within the gray matter and not in the white matter, as does pain from the periphery.

THE REPAIR OF ABDOMINAL INCISIONS

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WOUND repair and wound healing are a constant problem in surgery. The surgeon makes incisions in the abdomen more than in any other region. He should be concerned with the best methods of repairing these wounds. Every thoughtful surgeon is interested in the processes that insure the optimum healing and restoration of the abdominal wall to as nearly normal as possible.

With all the importance of this subject and the general interest of surgeons in their daily dealing with it, there is an astonishing dearth of accurate description of the technic of abdominal wound closure as compared with the repair of other wounds, especially of a plastic nature. William S Halsted,¹ in his epoch making paper in 1913, in which he presented the silk technic and its essential philosophy which he had developed at the Johns Hopkins Hospital, devotes only a short paragraph to the discussion of abdominal wound repair, but gives no details as to type of suture and method employed.

In 1932, Dr Arthur Dean Bevan² presented a paper before the American Surgical Association entitled "Abdominal Incisions and Their Closure." In this paper special stress was laid on the description of various incisions, and emphasis was placed on the closure, giving the details of a technic worked out by himself at the Presbyterian Hospital, in which retention sutures of silkworm gut were tied over pearl buttons. No definite figures were quoted, however, relative to the percentage of wound disruption and of postoperative ventral hernia following closure of these various incisions, but in other respects this is a most comprehensive discussion of the subject of abdominal incisions.

It is only in recent years that the frank and honest discussion of wound infection and abdominal wound disruption, as a result of the study of carefully recorded and analyzed hospital records in our best hospitals, has revived an interest in wound healing

The repair of abdominal incisions presents particular problems that are not met with in other wounds or other regions. These may be analyzed under the following headings:

(1) The peculiar arrangement of the flexing and rotating muscles, and the aponeurotic layers entering into the complex functions of the muscles of the abdominal wall (Figs 1, 2, and 3). The lateral pull of the oblique and transversalis muscles on the outer edges of vertical incisions is an almost daily, distressing observation in the closure of such wounds.

(2) The repaired abdominal incisions, especially those in the upper abdomen, are subject to peculiar stress and strain as a result of vomiting, coughing, hiccough, distention and the lifting and moving of the patient by the

attendants in the administrations consequent to the many daily physiologic demands and in nursing care. The sudden pain associated with the above factors increases the lateral pull of the rotating muscles, and increases intra-abdominal tension.

(3) The abdominal incisions are more frequently contaminated with virulent and necrotizing aerobic and anaerobic organisms than any others



FIG 1.—To show direction of muscle and aponeurotic fibers of superficial abdominal muscles (From Spalteholz 2nd edition)

Activated enzymes are at times in contact with drained incisions in patients requiring intestinal repair, followed by fistulae. These are factors which not only inhibit normal wound healing but may actually digest the tissues and dissolve the absorbable catgut sutures used in the repair. In such wounds the factors of increased intra-abdominal tension are most often associated, and it is in these patients that wound disruption and ventral hernia are most frequently seen.

(4) In many elderly or cachectic patients suffering from prolonged malnutrition and vitamin deficiencies, and requiring extensive operations for resections of malignant growths of the gastro-intestinal tract, the low serum protein content of the blood and the tissues prevents normal healing and unquestionably predisposes to wound disruption.

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(5) Because of the dread of the factors mentioned under the above headings, many surgeons believe that heavy suture material should be employed both in the layer repair and in the tension or reinforcing sutures. Heavy chromic catgut, in double strands, as high as No 2 grade, is used in many clinics. One has but to watch the inexperienced house surgeon or assistant pull up on these continuous sutures, or the heavy silkworm gut or metal re-

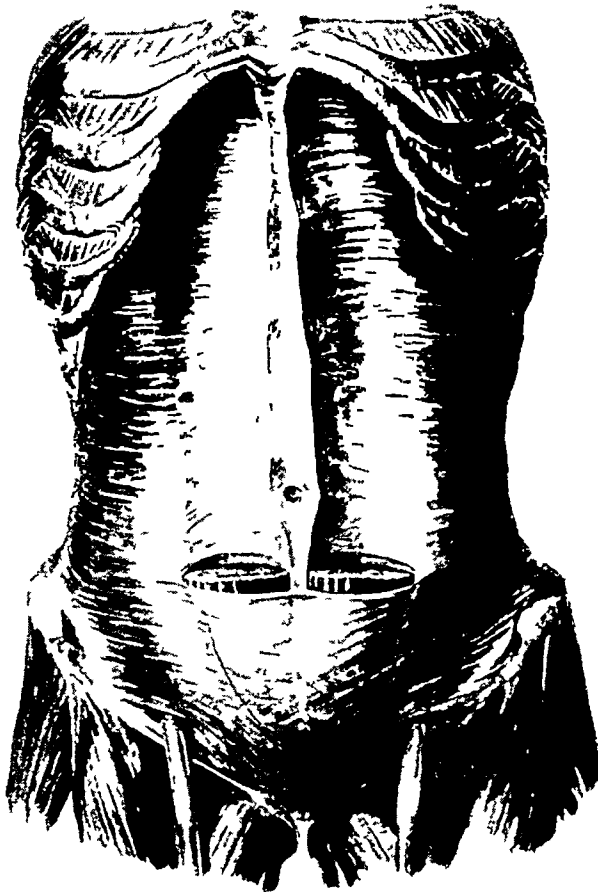


FIG 2—To show direction of muscle and aponeurotic fibers of deeper abdominal layers (From Spalteholz, 2nd edition)

inforcing sutures, to appreciate the amount of tissue necrosis that will inevitably result within the following 24 hours. A study of microscopic sections in wounds so repaired reveals long transverse lines of tissue necrosis on either side of the repaired incision (Figs 4 and 5). The necrosis takes place until the tension between suture and tissue is relieved. This tension, with a running continuous tight suture, diminishes the blood supply to the very tissues in which the surgeon is attempting to encourage wound healing. This mistake of tight suturing is probably the most common one made in the repair of abdominal incisions.

Because of the fear of wound infection, and persistent sinus formation resulting from employment of nonabsorbable sutures, catgut is used by the

majority of surgeons in abdominal work. In wounds contaminated with lower ileal and colon contents, nonabsorbable sutures should not be used, but in such wounds, contaminated with necrotizing organisms, and in incisions where activated pancreatic ferments are apt to be secreted, as in duodenal, jejunal and pancreatic operations, catgut has very definite drawbacks. The irregular and early absorption of both plain and chromic catgut sutures in



FIG 3.—To show direction and distribution of nerves to abdominal wall (From Spalteholz, 2nd edition)

the presence of intestinal ferments has been noted by every experienced surgeon and has been experimentally demonstrated.³ Another factor, which has only within recent years been pointed out,^{4, 5} is the allergic reaction of catgut in patients showing edema of the wound edges and in disruption of abdominal wounds. Kraissl,⁴ working in our Surgical Laboratory, sensitized 52 guinea-pigs to plain and chromic catgut. Celiotomies were performed upon these animals. Thirty per cent of these guinea-pigs disrupted their abdominal wounds. All of a series of 26 control guinea-pigs healed normally except one. There is little doubt but that the local reaction in patients allergic to catgut predisposes to infection and favors wound disruption.

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Contaminated Incisions With and Without Abscess—In abdominal incisions contaminated with ileal and colon contents our present technic is as follows. If an abscess, as in appendicitis, is present, it is drained with one or

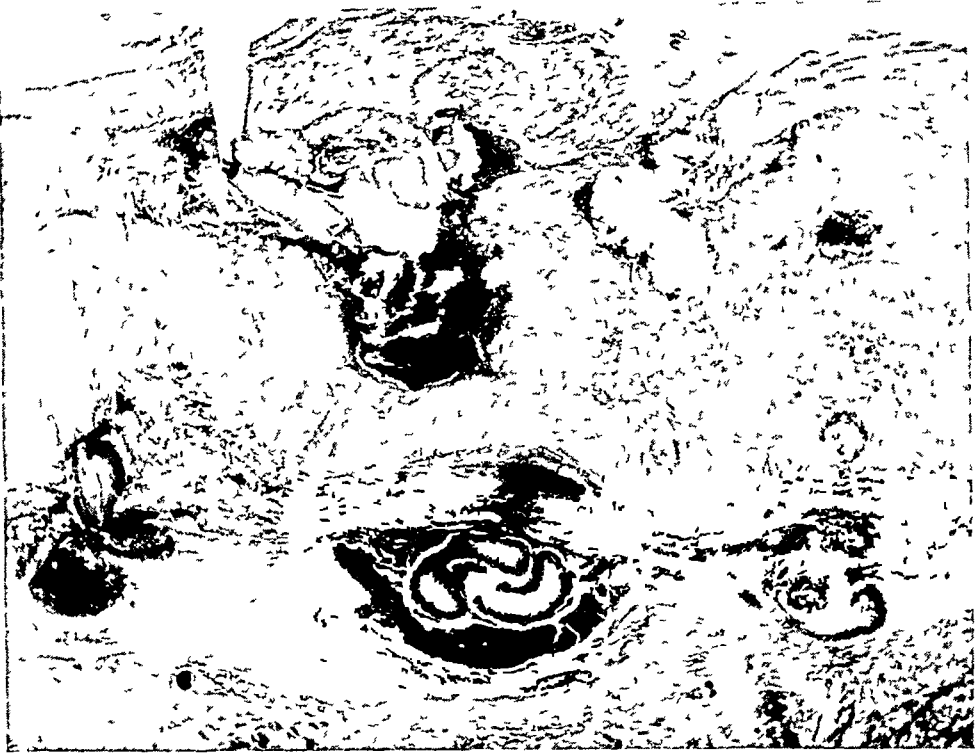


FIG 4—(Two day wound) There is a moderate amount of cellular infiltration around the catgut sutures, thick, swollen strands of which are seen to the left surrounded by exudate. On the right side are seen the silk sutures surrounded by practically no exudate. Fibroblasts and granulation tissue are already evident around both catgut and silk sutures. Repair has already started.

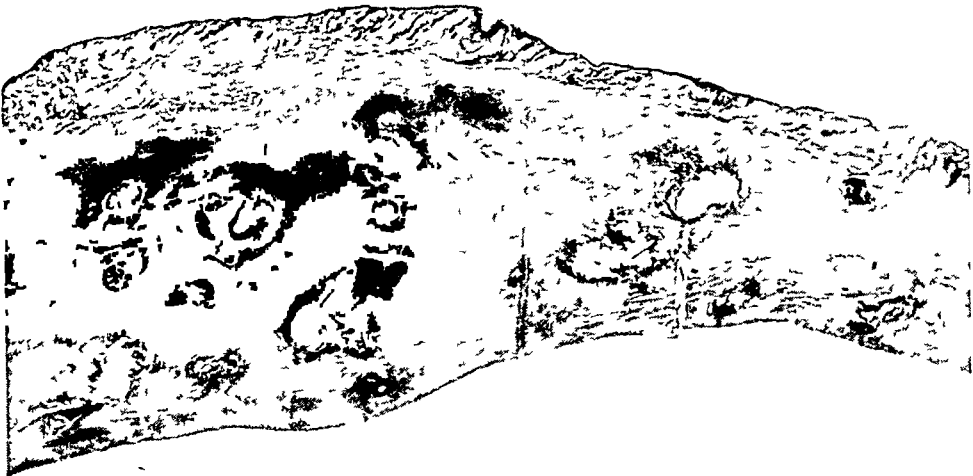


FIG 5—(Six day wound, catgut on the left side, silk on the right side) All silk fibers are separated by an ingrowth of fibroblasts and giant cells. In striking contrast there is no growth immediately around the catgut, which is surrounded first by a pool of exudate, then degenerated muscle, and then by granulation tissue on the outside of this. This is a very striking contrast. Note the difference in the thickness of the wall on the catgut and silk side, due to excessive edema of the tissues where catgut was used.

two soft rubber tubes or cigarette drains, introduced through a small opening in a China silk tampon, the peritoneum is closed with interrupted No. 00

chromic catgut sutures around the drains, and the wound is then packed with weak iodoform or zinc peroxide gauze around the drains inside the silk tampon. No attempt is made to suture the muscles, subcutaneous tissues or skin. The patient must be kept in bed longer than the ones with sutured wounds, until the wound has filled in with granulation tissue.

If an abscess is not present but the wound edges are contaminated with ileal or colon contents, as in an open resection, a small Penrose drain is placed near the site of repaired intestine, the peritoneum is closed about it, and at least the central part of the wound is tamponed as in the case of the abscess.

Clean Abdominal Wound Repair—We tend, more and more, to employ fine silk in all abdominal work. Frequently the hemostats are left on until the lesion in the abdomen is revealed, when either catgut or silk can be decided upon. They should not be used together, as it has been demonstrated⁶ that catgut favors the growth of bacteria in the wound, and in an infected wound, silk, unless in very fine grades, is more apt to act as a foreign body and cause protracted sinuses. The only abdominal wounds not associated with abscesses that we drain now are resections for gastric and colon cancers, cholecystectomies, especially where the cystic duct stump is not adequately peritonealized, and common duct drainages.

In upper abdominal operations we determine the type of incision largely by the width of the intercostal angle—using the transverse for the wide-angled, obese patient, and the split rectus for the narrow costal-angled, thin individual. We prefer transverse incisions because the lateral pull of the oblique and transversalis muscles tends to close rather than open the incision. This is graphically demonstrated in patients not thoroughly relaxed under anesthesia. Furthermore, the transversely cut rectus sheaths with their transverse fibers hold the sutures much more securely, and do not tend to tear out.

FIG 6—Closure of peritoneum and posterior rectus sheath of transversalis fascia

Because of our previous experience with disruptions, some five years ago we adopted a technic for abdominal wound closure which in our hands has practically eliminated, in our clean cases at least, wound disruption and post-operative hernia. In both transverse and vertical incisions, in both upper and lower abdomen, we have employed and are continuing to employ the following technic for closure. Peritoneum and posterior rectus sheath or trans-

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versalis fascia, continuous, fine C silk or No 00 chromic catgut followed at 2 cm intervals with interrupted sutures. This is done to bring a continuous

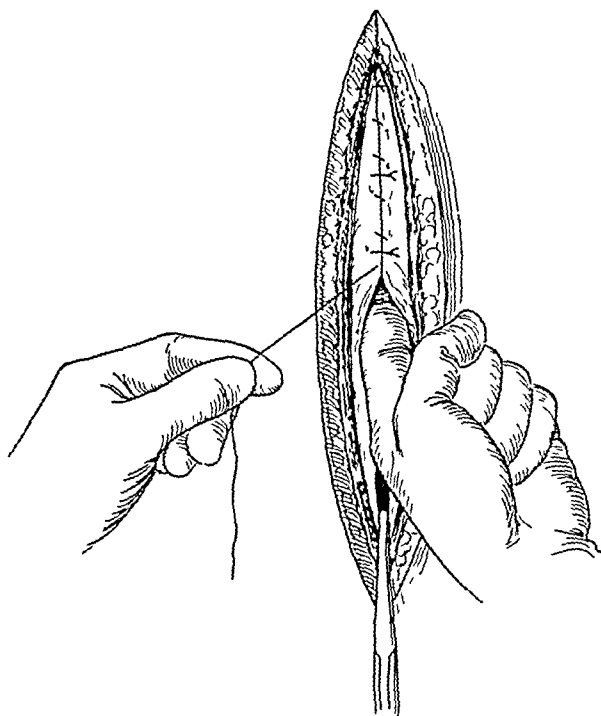


FIG 7—Showing the use of continuous fine silk followed by interrupted silk at 2 cm intervals

surface of peritoneum to peritoneum, to insure prompt agglutination of peritoneal edges, and to prevent possible projection or protrusion of omental tabs into the peritoneal repair (Figs 6 and 7). The anterior rectus sheath and oblique muscles (in the transverse incisions) are repaired with the same fine silk or chromic catgut by the use of a vertical figure-of-eight, or what we call the "far-and-near" stitch, at intervals of 7 to 8 Mm. This stitch is begun by introducing the needle 5 Mm from the edge of one sheath out through the margin of the other edge, into the margin of the first edge and out 5 Mm from the margin of the opposite sheath. Slight tension on the suture ends approximates the two edges of the sheath. These interrupted sutures should be tied loosely with a square knot, to allow for the take-up that results from the occurrence of the edema of repair, and to prevent any cutting of the sheath by the suture (Fig 8). This is a tensionless suture, if loosely tied, which prevents tissue necrosis, and therein lies its virtue. Proper hemostasis will obviate any need for subcutaneous sutures. The skin is closed with

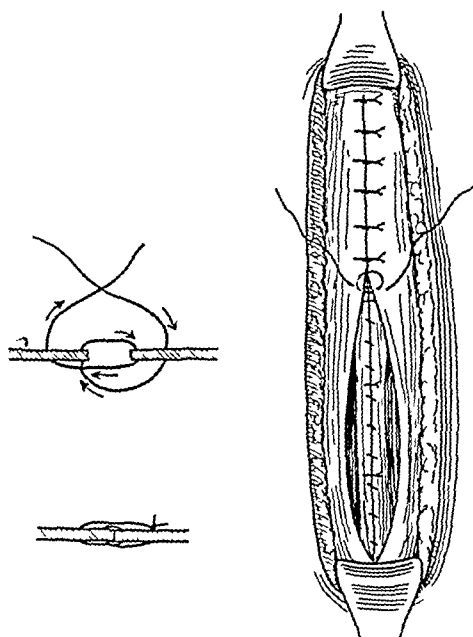


FIG 8—Closure of the anterior rectus sheath with "far and near" interrupted fine silk sutures

interrupted silk sutures on separate cambric needles to avoid the contamination of the silk by repeated puncture of hair follicles and sweat glands with the same needle and the same long suture (Fig 9)

We claim no originality in this technic, although we have not seen this identical procedure described Babcock⁷ describes this suture as "a combined relaxing and coapting suture, one of the best sutures for use where there is tension" Dr H H Lyle of St Luke's Hospital informs me that this "far-and-near" suture has been used for many years on his service, employing catgut, and that Thomas Markoe began using it for rapid closure of war wounds during the Civil War Dr Daniel F Jones used a similar stitch for

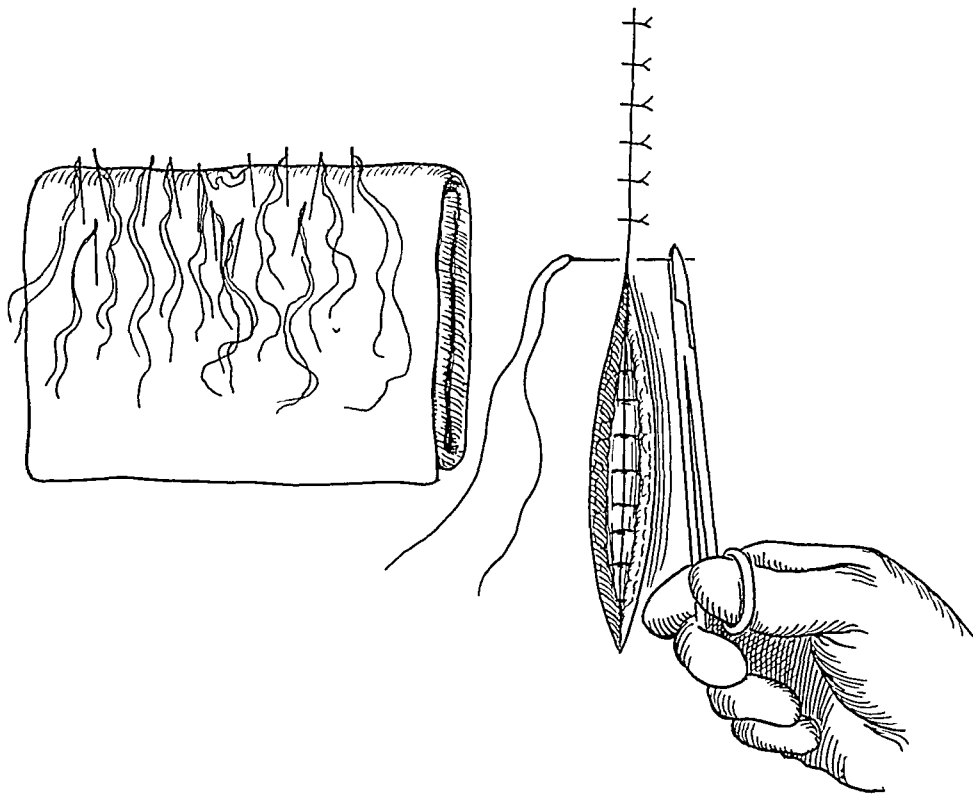


FIG 9—Closure of skin and subcutaneous tissue with interrupted fine silk on separate cambric needles

~~deep retention sutures~~—Undoubtedly it has been used by others, as we are using it, but we have failed to find a description of the technic for abdominal wound closure such as we are now employing. We do know it has reduced wound disruption and postoperative incisional hernia to a minimum in our postoperative and follow-up studies. For this reason we have abandoned the use of retention sutures which seldom proved effective, and frequently caused stitch abscesses.

In a control series of 300 abdominal wounds, with the layers closed with catgut, bolt retention sutures tied over pearl buttons were used in the great majority of cases. We first saw these pearl button retention sutures used in Bevan's Clinic at the Presbyterian Hospital, Chicago. Yet the incidence of

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wound infections, disruptions and postoperative ventral herniae was far greater (Tables I to V) Table VI shows the distribution of cases in the series reported and in the control group It will be observed that the number of biliary, stomach and bowel cases in the two series are roughly comparable, the numerical difference between the totals of the two groups being due principally to the number of appendicectomies and herniae in the reported series

TABLE I
THE INCIDENCE OF SUTURE MATERIAL AND THE TYPE OF
SUTURE USED IN THE ANTERIOR SHEATH

Material	No of Cases	F & N Suture	Plain Suture
Silk	300	228	72
Catgut	181	102	79
Control*	300	0	300
	—	—	—
Totals	781	330	451

* Cases in the control group were sutured with catgut

TABLE II
INFECTION IN CLEAN OPERATIVE WOUNDS

Material	No of Cases	Triv Inf	Per Cent	Ser Inf	Per Cent	Total Inf	Per Cent
Silk	199	4	2 04	0	0 0	4	2 04
Catgut	25	1	4 00	0	0 0	1	4 00
	—	—	—	—	—	—	—
Totals	224	5	2 22	0	0 0	5	2 22
Control	53	4	7 55	2	3 77	6	11 32

TABLE III
INCIDENCE OF DISRUPTION

Material	F & N Suture	Per Cent	Plain Suture	Per Cent	Total	Per Cent
Silk	1	0 44	0	0 0	1	0 33
Catgut	4	3 92	1	1 26	5	2 76
	—	—	—	—	—	—
Totals	5	1 51	1	0 66	6*	1 25
Control	—	—	13	4 34	13	4 34

* Two cases have not been included in which dehiscence of the wound took place, because the separation of the wounds only extended down to, but not through, the anterior rectus sheath

In our tables are included the abdominal incisions repaired, with the technic described, both with fine silk and fine chromic catgut, and a series of 300 cases repaired with chromic catgut in the usual manner, that is, with continuous sutures and reinforced with retention sutures We use the term trivial infection for any case in which the healing of the wound was not delayed

This includes single stitch infection or wounds with a serous discharge giving a positive culture. Serious infection is one which delays the normal convalescence and prolongs the bedstay of the patient.

TABLE IV
FOLLOW-UP STATISTICS

Material	Cases Followed	Per Cent Followed	Ave No Mos Followed
Silk	173	57.7	13
Catgut	111	61.4	17
Totals	284	59.2	15
Control	203	67.7	52

TABLE V
INCIDENCE OF POSTOPERATIVE HERNIA AMONG
CASES FOLLOWED

Material	No Herniae	Per Cent
Silk	0	0.0
Catgut	7	6.31
Totals	7	2.46
Control	30	14.77

TABLE VI
DISTRIBUTION OF CASES

Type of Operation	Silk	Catgut	Total	Control
Hepatic and biliary	81	81	162	140
Stomach and duodenum	40	25	65	57
Large and small bowel	16	48	64	42
Appendicectomies	23	21	44	3
Herniae*	52	0	52	7
Miscellaneous	88	6	94	51
Totals	300	181	481	300

* Including ventral herniae

Regular staff conferences and well organized follow-up clinics, in our best surgical services all over this country, have made the surgeons, especially the younger group, very critical of any statements regarding wound healing and postoperative herniae based upon impressions and not backed up by searching analyses of carefully kept records. Such studies have revealed a much higher incidence of disruption and ventral hernia in surgical services than the estimates based upon impressions.

Before closing I wish to emphasize again that if silk is to be employed in the repair of wounds, it must be used in the very fine grades. This connotes the minimal tissue damage by the use of sharp knife dissection, fine

hemostats, fine needles, complete hemostasis, absence of tight sutures, careful isolation of skin edges, and protection of exposed tissues from drying and air contamination

The number of recognized surgeons throughout the country who have adopted silk technic within the past five years is remarkable and speaks for their open-mindedness and their interest in ideal wound healing. It is regrettable that Halsted, who did so much to demonstrate the principles of wound healing, did not live to see the present renaissance of his philosophy.

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DISCUSSION—DR SAMUEL C. HARVEY (New Haven, Conn.) I am very happy indeed to have the opportunity of discussing Doctor Whipple's excellent paper. I shall not go into technical details but I wish to restate the problem in a more general way.

There are two ways, of course, of determining the certitude with which the healing of a wound may take place. One is by experimental investigation upon animals, and the other is actual surgical practice. Both of these are essential for our knowledge of the healing of wounds.

From the experimental work upon animals, we have learned that the healing of wounds follows a normal process. It is a biologic phenomenon, which corresponds to the laws of growth in all biologic things.

We have also learned that there are certain things which interfere with the normal healing process. The process is, in the first place, one of cleaning up tissues which have been devitalized—a matter of three or four days. The secondary part of the process, and the most important, perhaps, is the restitution of the tensile strength of the wound by the growth of the fibroplastic cells.

Theoretically, such a process should take place to the best advantage when there is the least amount of destruction of the cells, when there is no infection, and when there is no foreign material introduced in the wound. Frankly speaking, we have to compromise, because a wound has to be carefully approximated in order to obtain healing. This means that we have to use sutures.

The use of sutures introduces foreign material into a wound. It is just as much the introduction of foreign material as is the devitalization of the cell, the introduction of infection, or the forming of hematoma and serous

accumulations Therefore, it must be reduced to the absolute minimum in respect to the type of material and in respect to the quantity necessary to achieve the purpose of obtaining approximation of the wound

Experimentally, that means the reduction of the suture material in size to a minimum and the use of suture material which has the least irritative effect in the wound Clinically, the same thing follows from studies of the complications of wound healing

I would like to point out more emphatically than Doctor Whipple perhaps did that no one is really in a position to evaluate the healing of a wound clinically unless he has very carefully, and at the time, personally studied the healing of his own wounds The impression which all of us may have, that our wounds heal all, or practically all, without any complications, is, I am convinced, a completely erroneous one A careful follow-up and careful evaluation will show, I think, that 4 or 5 per cent, as a minimum, do not heal as perfectly clean wounds

A measure of that, perhaps the most characteristic and vital measure, is the disruption of the wound Again, if one studies very carefully his cases as they come along, he will find a very definite incidence of disruption I do not think there is any exception to that

Perhaps more important, with a follow-up he will find that there is a definite percentage of postoperative herniae, and a postoperative hernia is, I think, almost without exception, a disruption of the wound, in most instances not involving the skin but the underlying structures

Therefore, it seems to me that Doctor Whipple's experience here is a very pertinent one and very much to the point because he has carefully carried over into the clinic the indications resulting from his experimental work

By the criteria of a careful follow-up and study of his wounds, and with the actual decrease of the complications of healing obtained by the use of a nonirritative suture material, in fine and restricted quantities, with the necessary delicate technic that is required, he has actually demonstrated a very significant decrease in the complications of wound healing

I should like to add this one thing, however, for those of you who wish to follow this procedure you should go back to Halsted's article, in 1913, in which he gave the details absolutely essential for the successful carrying out of this technic

DR ALBERT O SINGLETON (Galveston, Tex.) Doctor Whipple is to be congratulated upon his management of this very troublesome vertical, upper abdominal incision I do not know of anyone who has succeeded so well with it There is no controversy that I can see about his technic and the reason for his employing it We have approached this subject from a little different angle and have tried to use a more anatomic incision, more or less upon the principle of the incision advocated some years ago by Sloan¹

The chief strain or tension upon the abdominal wall, in the upper abdomen particularly, is in a transverse direction, due to the action of the lateral abdominal muscles The chief holding material of the abdominal wall is the posterior sheath of the rectus muscle, which is the tendinous continuation of the internal oblique and transversus muscles If this is cut vertically across its fibers, the difficulty of maintaining it in position is very great, and when an unusual strain such as coughing and vomiting, it probably is impossible to maintain it in position

On the other hand if this structure is cut transversely in the direction of its fibers, it may be split across the linea below, and by retracting the rectus muscle out of its sheath on either side, sufficient room may be acquired for

almost all operations upon the stomach or gallbladder, *etc* When the wound is closed, its edges automatically come together. No tension is required to coapt them, and thus no strangulation of the tissues can occur.

This same principle may be employed in an incision we are using lateral to the rectus muscle, in which the rectus is retracted medially. This incision is employed on the right side for operations upon the biliary passages, and on the left side for operations upon the splenic flexure of the colon, and particularly for splenectomy. It begins near the midline, three to four inches above the umbilicus, and extends obliquely downwards and outwards, just below the rib margin, almost to the iliac crest, just posterior to the anterior superior spine. This is in the direction of the fibers of the internal oblique muscle. The anterior sheath of the rectus muscle is cut transversely and the muscle freed from the sheath for a short distance above and below. The incision is continued across the fascia of the external oblique for two to three inches in line with the skin incision, and the external oblique is retracted further, laterally. The rectus muscle is retracted toward the midline, and its posterior sheath is split from the linea alba, laterally, into the internal oblique and transversus muscles. The internal oblique is split and the transversus and peritoneum cut in the same incision. This gives a very advantageous exposure of the gallbladder, bile ducts, appendix and pyloric end of the stomach on the right side. The wound comes together without tension and is quickly and easily sutured in layers.

The incision may be used to advantage on the left side in operations for removal of the spleen, and affords a better exposure than the usual incisions and with no danger of disruption or weakening of the abdominal wall.

Our experience, as indicated here by a review of 710 consecutive upper abdominal incisions, is that, of the vertical incisions, 284 had nine disruptions, or 3.2 per cent, 15 herniae occurred, or 5.3 per cent. Of 426 transverse incisions (if I may call these transverse), we had no disruptions, and only one hernia was found, which occurred in a patient who had had an omentopexy performed for cirrhosis of the liver.

The suture material in these cases was not investigated. We know that disruptions occurred in the first series of vertical incisions in which silk was employed in conjunction with plain and chromic catgut. The suture material which has been used in these 426 cases has been either plain No. 1 catgut or No. 0 chromic catgut.

The time required for making the incision is longer but the patient is more comfortable following the operation, and the sense of security in the mind of the surgeon makes the extra effort well worth while.

REFERENCE

- ¹ Sloan, G. A. A New Upper Abdominal Incision. *Surg. Gynec. and Obstet.*, 45, 678, 1927.

DR. HOWARD LILIENTHAL (New York City, N. Y.) Speaking only of perfectly clean wounds, it must be obvious that an infection in a perfectly clean wound is usually carried in by the scalpel.

I do not use a scalpel. I use the diathermic knife, the electrical scalpel. It has to be used with care, speed and precision, and thus obviates infection from the skin, even the deeper layers.

DR. ROSCOE R. GRAHAM (Toronto, Canada) An analysis of our wound infections and wound disruptions has shown a higher incidence than in the series which is being reported by Doctor Whipple. While Doctor Whipple is placing great emphasis on the type of suture material, and making a plea for

the efficacy of silk in wound closures, the actual type of material is probably not as important a factor as he would lead us to believe. One has but to see Doctor Whipple operate, to recognize the gentleness and care with which he treats tissues, and this I think, in no small way, has contributed to the excellence of his results. In our own series we have had no incidence of wound infection in which there was not evidence of an accumulation of serum or imperfect hemostasis in the wound. The former we believe is due to massive ligatures or traumatic methods in opening the abdominal wall. In other words, meticulous, sharp dissection, having regard for anatomic structures and planes, the avoidance of mass ligatures, and the securing of perfect hemostasis are probably the important factors in securing firm, primary healing of abdominal wounds. These above requirements must of necessity be fulfilled if the surgeon employs silk, and in this regard, the use of silk making necessary such a type of technic constitutes its greatest virtue.

DR WALTER D WISE (Baltimore, Md) I would like to call your attention to a subject that I hesitate to bring before this Association, except to pass it through this organization to many of the younger surgeons. It is about the matter of knots.

One constantly sees, if one is alert to that subject as some of us have been taught to be by avocations instead of vocations, particularly that of sailing, the indifference with which surgeons tie knots. Speed, it seems, is what they are endeavoring to accomplish rather than meticulous care in tying a flat or reef knot.

This does not apply, of course, so much to silk as it does to catgut. In the use of silk, a granny knot will hold quite well, but it is not entirely reliable. In the use of catgut, anyone who has watched it swell and untie itself will realize that it is essential, not only to tie a reef knot, but to use a third throw.

What I am saying does not apply only to closing incisions, but it applies more particularly to the ligation of vessels, and probably accounts for some of the catastrophes.

It is probable that a good many disruptions of wounds, as has been hinted at but not actually said this morning, occur in the first day, or probably during the first hour or two after an operation, resulting from the act of vomiting or straining. That is the time, regardless of when the catgut digests or if there is any allergy or any other factors involved, when one wants the knot to hold. If the knots are tied with the indifference that one sometimes sees, then this may account for some instances of disruption.

DR JOHN J MORTON (Rochester, N Y) I would like to endorse Doctor Whipple's discussion on the healing of wounds because I have been using practically an identical technic during the last five years. I think that it should be emphasized that he does not make use of so-called retention sutures. I have given up using retention sutures also. The use of very fine silk, C grade, provides for accurate approximation of the divided tissues. There is one difference, however in our technic. When we make a vertical incision, we go to the edge of the rectus muscle and retract the rectus over, so that we have our incision staggered and bolstered by the rectus muscle in front. I think this may help in some cases when postoperative distention occurs.

I have been very much pleased with this type of closure and I use it in gastric and gallbladder surgery as a routine. It is used on a good many other lower abdominal cases and even in some large bowel resections, when I am reasonably sure that there has been no major contamination.

DR HARVEY B STONE (Baltimore, Md) There is one factor which has been mentioned only passingly, and which I think needs at least a word of

reference that is, those cases of wound disruption which occur, apparently due to a failure of the healing power of the tissues, and which I believe in some instances have no relation either to the type of incision made or the material employed in the suture, or any of the other defects which have been mentioned previously

I am confident that there are wounds which for some unknown biologic reason do not heal and I think in those cases, no mere technical procedure is going to correct that failure

In the past, it has seemed to me that the incidence of such wounds has been strikingly high in patients suffering with advanced malignant disease, and in old age, conditions in which the recuperative power of the tissues is naturally lowered. These disruptions often take place in wounds 10 to 12 days after operation, when everything seems to have been progressing normally. The wound suddenly splits open during an attack of coughing or sneezing, when one examines the wound edges, they appear as though made only a day or two before, without any evidence of effective granulation

Since the routine employment of blood transfusion in operations for malignant disease, it seems to me that the incidence of such disruptions has been remarkably decreased. One might infer that there was a factor that might be detectable in such cases, such as a diminished blood protein as suggested by Doctor Whipple, or some other dyscrasia, that accounts for this failure to heal. Only yesterday, I saw a patient who had had a small fibroma of the skin removed two weeks previously from the thigh, a small wound, two or three inches long, closed with silk. It had apparently healed and the dressings had all been removed. On the thirteenth day, the patient, while driving an automobile, simply cracked the wound wide open, throughout its entire extent. It didn't bleed much, and the cut surfaces looked almost as fresh as though it had been made just the day before.

DR HUGH H. TROUT (Roanoke, Va.) There are a great many objections to the use of catgut, one of which has not received the attention it deserves. For example, for years we have been thinking that the degree and rate of absorbability of catgut were dependent largely upon chromic or tannic acid. The factor to which I refer is the age of the animal from which the gut is removed.

Our attention was first called to this by the report of Bulloch on Suture Material, made to the Royal Society of Surgeons of England. Since this time we have been doing considerable experimental work, trying to obtain a substitute for catgut, as well as test the absorbability of the various brands and sizes of catgut. Naturally, we have found that the older the animal the less absorbability the gut has. In fact, if one takes an old ram, the gut removed is practically a foreign body. Apparently it is impossible for the manufacturers to know definitely the age of the animals from which the gut is removed.

DR CHARLES C. LUND (Boston, Mass.) Doctor Stone's remarks have stimulated me to enter this discussion. The work that I am going to mention is so incomplete that I was not planning to say anything about it at this meeting.

As many of you know, Wolbach and others, in 1926, demonstrated that wounds in animals with scurvy will not heal. Recently, determinations of blood vitamin C, the active principle in orange juice, have become reasonably easy to make and are reasonably accurate. At Doctor Cutler's Clinic and in London, it has been shown that the great majority of patients that were being

treated for gastric ulcer have a very low blood vitamin C. Some of them practically have scurvy.

At the Boston City Hospital, on our service we have now made something over 1,000 determinations on several hundred patients with miscellaneous surgical conditions. We cannot report any results as yet, except to say that in the population there are a great number of people of all classes who are running suboptimum levels of vitamin C, many of the levels apparently close to scurvy. Of course the level of serum protein, as mentioned by Doctor Stone, is also important in wound healing.

I think that vitamin C is probably also very important. I will say, however, that the first disruption that occurred in a patient who had a blood vitamin C determination made had an absolutely normal level. We checked up with the house officers and we found that, according to the requirements set forth by Doctor Whipple, this wound had been very, very badly sutured.

DR PHILEMON E. TRUESDALE (Fall River, Mass.) Doctor Wise has called our attention to the undesirability of knots in wounds. There is a distinct disadvantage in leaving a field of operation studded with knots, especially when the material is chromicized catgut. The knot acts as a foreign body. After taking cultures from the wound before secondary closure, it will invariably be found that the wound is infected, if at all, around the knot. Bacteria may be found in the region of the knot and nowhere else.

There is always some degree of round cell infiltration at the point of fastening. The coarser the ligature, the greater the reaction. On the contrary, a knot which has been tied with fine silk or plain catgut produces very little reaction. A knot tied with No. 1 or No. 0 chromic catgut causes only a mild reaction, with a few bacteria, but when a No. 3 or No. 4 chromic catgut is used, there follows a marked reaction around the ligature. That is why at either end of the wound one frequently feels a hard, tender swelling, due to inflammatory reaction around the ligature.

DR ALLEN O. WHIPPLE (closing) Regarding the results that Doctor Singleton has obtained by the incision that he uses. We have employed this incision in a number of upper abdominal cases and for gastric work, particularly around the pylorus, and we have found it an exceedingly good one.

In regard to the use of the electric cutting current. We have employed this at times, but it always seemed to me that there was more of a margin of tissue necrosis, even though the current is used quickly, as Doctor Lihenthal has suggested. We still prefer the scalpel incision.

Relative to knots, I am sure that all that has been said is correct about the tying of knots. Certainly in fine suture material, whether it be silk or catgut, a knot can be tied more securely and with less foreign body reaction than when the heavier grades are employed.

I did speak about the low serum protein in the cachectic individual with very poor wound healing. I am sorry that I did not bring that observation out more fully. Many of the points, because of the time, I was not able to deal with as fully as I would have liked to.

Doctor Harvey and Doctor Morton have really touched upon the important feature of wound healing, and that is. That in order to get optimum wound healing, whether one uses silk or catgut, one must minimize the tissue damage, and if one uses silk, the philosophy that goes with it develops inevitably and tends to minimize constantly tissue damage.

SPONTANEOUS RUPTURE OF THE SUPERIOR AND INFERIOR EPIGASTRIC ARTERIES WITHIN THE RECTUS ABDOMINIS SHEATH

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SPONTANEOUS rupture of the internal mammary or epigastric vessels within the rectus muscle is a definite surgical entity, though rarely occurring, and hence lacking the familiarity characteristic of the average abdominal lesion. Examples of this condition are appended.

CASE REPORTS

Case 1—Male, age 55, had been driving an automobile over smooth roads for about four hours, after which time he turned the wheel over to his wife and settled back in the seat to rest his eyes and take a nap. Without any accountable reason, he suddenly became conscious of a mild, but sharply acute pain in the left side of his abdomen. This pain, at the end of 30 minutes, had increased to one of marked severity and the patient, being a doctor, feared that he had suffered an intestinal rupture or possibly a mesenteric thrombosis. There was no great shock, but he became nauseated and vomited. Two hours elapsed from the onset of the symptoms before he reached his home and received medical attention. The attending physician made a tentative diagnosis of some acute intra-abdominal lesion. He was taken to the hospital immediately, and was seen by the author shortly after admission.

Physical Examination disclosed a heavy-set, stout man, suffering with very acute abdominal pain, so severe that he could not tolerate the weight of the bed clothes on his abdominal wall. There was a mass in the region of the left rectus muscle at about the level of the umbilicus which was exquisitely tender on palpation, and appeared to be about the size of a grapefruit. The left rectus muscle was tensely rigid above and below the mass, but the rigidity seemed to stop with a clear-cut line of demarcation along the midline of the abdomen, and the right rectus and right half of the abdomen were neither tender nor rigid. The left side of the abdomen showed some tenderness and rigidity spreading out into the oblique and transversalis group of muscles, but these phenomena tapered off completely before reaching the anterior superior spine of the ilium. Temperature, 100.6° F, pulse, 120, blood pressure, 175/95. R B C, 4,500,000, hemoglobin, 90 per cent, W B C, 14,000, polys, 82 per cent. The bleeding and coagulation time were normal, and there was no reduction from the normal in the platelets.

The abdomen was not distended. Nausea and vomiting had ceased, there was no mass to be felt by rectum, and the urine was negative for red blood cells and pus. Careful consideration was given to the possible diagnosis of incarcerated hernia, volvulus, mesenteric thrombosis or a ruptured viscus. Roentgenologic examination, made in both the supine and prone positions, revealed no evidence of subcutaneous emphysema or free air in the peritoneal cavity. *Diagnosis* Spontaneous hemorrhage in the left rectus muscle.

Operation—An incision six inches long was made through the skin overlying the left rectus muscle, with the center of the incision at about the level of the umbilicus. On reaching the anterior sheath of the rectus muscle, there was immediately observed an extensive ecchymosis with dark discoloration such as one would see underneath the peritoneum overlying a ruptured, ectopic pregnancy. Incision of the anterior sheath of the rectus disclosed a large, blood-filled cavity in which one could easily pass the entire hand both upward and downward. A quart of clotted blood was removed, and several bleeding vessels were found and ligated. Two of these bleeding vessels spurted,

one from above and one from below, and were thought to represent the anastomosis between the internal mammary and epigastric arteries. The rectus muscle appeared badly mutilated as a result of this rapidly dissecting hematoma. Much of the muscle had already undergone separation and pressure necrosis. The wound was closed except for one small Penrose drain for 48 hours. Recovery was uneventful.

Case 2—White, male, age 64, was admitted to the hospital with the history of having had a slight pain in the left lower abdomen during the previous week. On the day of admission the pain had become suddenly and acutely severe, and had been continuous since the exacerbation began. The sudden development of pain occurred while the patient was at the breakfast table. He had taken no undue exercise since arising from bed, and there was no history of direct or indirect trauma. He had been nauseated for several hours before admission, but there had been no vomiting.

Physical Examination—The abdomen was flat and scaphoid except over the left rectus muscle which stood out prominently from the symphysis almost to the ensiform, like a large Bologna sausage. The area of distention seemed to be absolutely limited by the external and internal boundaries of the sheath of the rectus muscle. Rigidity was board-like, whereas, the oblique muscles to the outer side and the right rectus and right half of the abdomen were soft and flaccid. There was a history of the patient having stuck a nail in the plantar surface of the left foot eight days previously. Temperature, normal, pulse, 72. R B C, 4,100,000, W B C, 10,600, polys, 80 per cent. There was no increase in any of the reflexes, and no spasm or stiffness of the jaws or neck. The normal temperature, moderate leukocyte count, and the slow pulse were not in keeping with an acute intra-abdominal condition. Because of the history of a puncture wound of the foot eight days previously, it was thought that this might possibly be a case of localized tetanus. The wound in the foot appeared to be completely healed, and showed no tenderness or inflammation, it was, however, opened by blunt dissection, but no evidence of inflammation, serum or pus was found. Cultures were taken from the wound and tetanus antitoxin, 1,500 units, injected around the wound, 20,000 additional units were given in the vein, and 20,000 in the muscle. During the next four days 280,000 more units of tetanus antitoxin were administered, during which interval of four days there had been no change in the patient's condition. There had been no further evidence of tetanus, and the culture from the wound in the foot was negative at the end of five days.

The left rectus muscle had, however, become more tense, and more sensitive, necessitating the administration of sedatives and opiates to control the pain. There then appeared a slight, globular swelling at about the center of the left rectus sheath, aspiration of which disclosed old, dark blood which proved negative on culture. In the meantime, the patient had developed a rather septic type of temperature which ranged from normal in the morning to 103° F in the evening. The bleeding and coagulation time were normal, platelets, 275,000, leukocytes, 7,100, polys, 72 per cent. Blood pressure, 148/88. It was evident that the patient had been upset by the large doses of tetanus antitoxin administered because of an erroneous diagnosis.

Operation—An incision five inches long was made over the center of the left rectus muscle. The sheath was almost black from hemorrhagic extravasation, upon incision of it there was evacuated a large quantity of old, broken down and liquefied blood clots. The entire rectus muscle adjacent to the incision seemed to be completely destroyed by pressure necrosis, and by dissection of the hemorrhage upward and downward between the muscle fibers. There was only one bleeding vein seen, and this followed the enucleation of some of the organized, old adherent clot. Cultures from the cavity in the rectus muscle showed colon bacilli and unidentified Cocci after three days. The patient was immediately relieved of his pain. The temperature became normal, and convalescence was rapid and uneventful.

Case 3—Female, age 46, was referred to the author by her family physician, who thought she had a pelvic tumor on the left side which was undergoing degeneration because of a mass, the presence of acute tenderness, and some little fever. The patient was

a multipara whose menses had been perfectly regular, and there was no pelvic dysfunction or symptoms of pelvic disturbance in her history. She related that this trouble began with pain in her lower left abdomen one week previously, and that it had steadily progressed until she appreciated that there was a tender mass in her lower abdomen on the left side.

Physical Examination of the pelvis showed a normal cervix by inspection, and bimanual manipulation disclosed the uterus to be freely movable, no tenderness in the cul-de-sac, or in her broad ligaments. The pelvis to the right of the midline was soft on pressure, but a large mass was palpable to the left of the midline, and was very tender, this tumor could only be indefinitely appreciated by the fingers in the vagina.

On abdominal examination, there was at once observed a crescentic area of purple ecchymosis extending below the umbilicus for about two inches, and which was confined entirely to the lower half of an imaginary circle drawn around the umbilicus. The patient was questioned carefully as to how she had gotten this bruised area in the skin. Any history of injury or any other predisposing cause was denied by the patient. Furthermore, she did not know that this area of discoloration existed. Further examination disclosed a mass about the size of an orange lying apparently within the rectus sheath between the level of the umbilicus and the pubic bone. The mass was movable, and quite tender, while the muscles to the right and left of the mass were perfectly soft and not painful to pressure. Upon asking the patient to assume a half sitting posture, it immediately became apparent that the mass became more prominent and was apparently located in the anterior abdominal wall. The ecchymosis around the umbilicus was the real clue to the diagnosis of hematoma in the rectus muscle. It was assumed that some of the blood from the hematoma had dissected down below the semilunar fold of Douglas, and then had gravitated along the obliterated hypogastric artery upward to the umbilicus. Operation disclosed an hematoma in the lower rectus sheath, this had become organized, and when enucleated was about the size of a small orange. The patient was immediately relieved of her pain and made an uneventful recovery. Before leaving the hospital, and after a most careful questioning, she finally thought that perhaps the beginning of this trouble was a sneezing spell. However, she was not positive in her statements, and it did seem that this case should be considered a spontaneous rupture of the vessels.

Symptomatology—In spontaneous rupture of the epigastric artery, the patient usually complains of a sudden, severe pain to the right or left of the midline, and usually at about the level of the umbilicus. However, premonitory soreness of mild character lasting from six to seven days has often been described preceding extensive vascular rupture with massive hemorrhage. This type of onset has been observed in several cases, notably those reported by McCarty,¹ Culbertson,² and in one of the author's cases. With the rapid development of massive hemorrhage the pain is usually very severe, and the patient will not tolerate the weight of clothing or any extensive manipulation in the examination. There is usually a normal or slightly increased temperature, and a moderate leukocytosis. There is usually some prostration, and frequently prolonged nausea and sometimes vomiting. There is usually a localized mass, exquisitely tender to palpation, and described in many reports as varying in size from a hen's egg to that of a large grapefruit. The mass is always confined to the sheath of the rectus muscle, but it must be remembered that there is no posterior sheath below the semilunar fold of Douglas, and hence blood may extravasate downward anterior to the peritoneum.

Several cases reported have shown the hematoma to have pushed the anterior peritoneum inward until the mass could be palpated per vaginam.

Ecchymosis is a most important sign, and frequently offers the first intimation as to the correct diagnosis (Case 3). Vernon³ reported a case with suggillation about the pubis and perineum. One of the characteristic features about the mass is that it does not change its position, and always appears fixed in the right or left abdominal wall.

Fothergill⁴ contributes a sign which was demonstrated in Case 3. If the recti muscles are made to contract by having the patient sit partially up, the mass can still be felt and yet it cannot be moved to either side of the abdominal wall. The absence of rigidity and tenderness in the abdominal wall adjacent to the tumor is almost pathognomonic of a lesion in the rectus sheath, in contradistinction to what would be expected if there were an intra-abdominal lesion present. Tenderness, tonic contraction on one side, and absence of surrounding rigidity are definitely characteristic of this lesion.

The differential diagnosis is considered very important by most authors writing on this condition. They seem to feel that the lesion has been too frequently diagnosed as an acute intra-abdominal lesion. It is true that in many of the reported cases the preoperative diagnosis has been mesenteric thrombosis, intussusception, volvulus, incarcerated hernia, gallbladder disease, twisted ovarian cyst, ectopic gestation, and degenerating fibroids of the uterus. McCarty feels that it is particularly important to recognize the possibility of this condition being associated with pregnancy, lest there be confusion with an ovarian cyst or a pedunculated fibroid, as cases have been reported occurring during pregnancy, labor and in the puerperium.

Etiologic Factors—This covers a rather broad field of assumption. Many cases, however, are reported to have had as a contributing factor, coughing, sneezing, and any severe jolting associated with sudden muscular contraction. Some cases have been reported in association with infectious processes such as tetanus, tuberculosis, typhoid and typhus fever, influenza and low states of muscular inanition, such as is found in chronic ulcerative colitis. It seems quite reasonable to expect that a weak, atrophic muscle would require less effort to produce either a tear of its fibers or rupture of the blood vessels. Conversely, one might intelligently inquire whether atrophic muscles are capable of contracting sufficiently to produce rupture of the normally elastic vessels.

Degeneration of blood vessels must also be considered an important contributing factor, and it is to be remarked that in practically all of the cases reported, the individuals are usually in late middle life, and all showed evidence of sclerosis and vascular degeneration as indicated by varying degrees of hypertension. In 50 case reports, personally reviewed, the average blood pressures were 170/95. One would expect muscular atrophy and vascular degeneration to be present in association with some infectious processes, particularly in men leading a sedentary life, and in inactive women, especially during pregnancy and the puerperium. As indicative of how little may be

the contributing factor, Halperin⁵ reports the occurrence in a woman, age 71, resulting from raising up as she turned over in bed. As a rule, however, no definite cause can be found for the so-called spontaneous case. Malpas⁶ thinks that the spontaneous ruptures are due to some latent blood dyscrasia. He reports two such suggestive cases. Evidence of this condition was not present in my patients, and was noted in only three of the other cases reported in the literature. Many authors think the contributing factor is a pendulous abdomen, which produces traction upon the vessels and thus induces chronic attenuation and friability. A considerable effort has been made by many surgeons to study the histologic pathology of the muscle and vessels found at the time of operation, the most characteristic findings have been old hemorrhage, lymphocytic infiltration and necrosis. On the other hand, Trofimoff¹⁴ and numerous others could find no satisfactory explanation in the excised muscles and vessels involved in the hematoma. Nørgaard¹⁵ studied 72 cases in which the correct diagnosis was made in only 11 instances. The only contributing cause he could determine was a low capillary resistance and in two cases a prolonged bleeding time. Giardina¹⁶ records one case in a syphilitic who had an associated pyloric ulcer, the microscopic studies from the hematic area in the rectus showing a chronic productive myositis. One of our cases showed a localized arteritis and peri-arteritis (Case 1), and a number of case reports have recorded arteriosclerosis or hypoplasia of the vessels, including focal degeneration of muscle and vessels following infections. Two reports showed aneurysmal dilatation, calcification and atheroma in the inferior epigastric arteries.

Quite an important group are those occurring in pregnancy, during parturition, or soon after delivery. Spirito¹⁷ and others have reported the sudden development of a hematoma in the rectus muscle occurring 15 to 30 minutes after the expulsion of the placenta, while Maxwell¹⁸ reports 12 spontaneous cases occurring during pregnancy, and 46 cases from other causes, in none of which was correct diagnosis made before operation. The frequent occurrence in multipara is in keeping with the theory of muscular stretching and impairment as a causative factor, the acute lesion being ushered in with an episode of coughing or sneezing. Jaschte and Meldolesi¹⁹ note arteriosclerotic changes in the epigastric vessels, especially after repeated pregnancies. To controvert this, Dencks²⁰ observed an instance which fell in this category in a woman, age 65, and attempted to determine the pathology of such cases by examining the histology of the epigastric arteries and rectus muscles in 95 cadavers of both sexes ranging in age from 50 to 90. The findings were not outstanding. Some arteriosclerotic changes were determined, but were not of such localized high grade character as to indicate enough friability to be conducive to spontaneous rupture.

Infection has played an important part in the study of the localized pathology. Chaher and Vallery²¹ reported an infected hematoma of the rectus muscle following typhoid fever in which the cultures showed Eberth's bacillus. Kenwell²² reported an infected hematoma in which the cultures demonstrated

Staphylococci aureus hemolyticus Wehik²³ reported 20 cases that he had collected of infected hematmata, but does not mention the infecting organisms. Harris,²⁴ operating under a mistaken diagnosis of acute appendicitis, found an infected hematoma of the right rectus muscle, and cultures disclosed a gram-positive *Bacillus* which was not identified. Delay in diagnosis and in operative treatment results in liquefaction of the hematoma with secondary infection of the clots by *Staphylococci* or the colon groups as demonstrated in Case 2. Influenza is the most outstanding infection found associated in the various case reports reviewed, hematmata having developed in the rectus muscle as a complication.

With²⁵ drew a most interesting conclusion in a case studied and operated upon by him. He thought the underlying factor was a hemorrhagic diathesis due to C avitaminosis. Study of the blood in this case showed a total absence of ascorbutic acid. No estimation of vitamin C in the urine was made. Several authors have thought that systemic disease had an important bearing on the development of the hematoma. Lehman²⁶ reports a case associated with splenomyelogenous leukemia, and Dlugi²⁷ reports the development of a hematoma in the left rectus muscle, which produced intestinal obstruction in a case known to have leukemia. Del Carril²⁸ also records a case of intestinal obstruction, occurring in a three months old child, due to extraneous pressure from a large hematoma in the right rectus muscle. Lenner²⁹ records a most interesting case, occurring after a Pfannenstiel incision, and says "There have been other reports of hemorrhage into the rectus sheath after Pfannenstiel's incision." It seems sound to conclude that hematoma of the rectus develops as a result of three causes: (1) Muscular effort, (2) following low-grade infection, and (3) spontaneous rupture due to focal degeneration of muscle and vessels.

The military surgeons of France, Germany, Austria and Russia have all recorded numerous cases following sudden muscular effort connected with military training. They conclude that rents of small vessels generally produce slowly growing tumors and a gradual exacerbation of symptoms. Rents of a large vessel produce a rapid development of symptoms and the pathognomonic signs are acute and definite. In this connection, Brendeau³⁰ reports a rapidly developing hematoma in the rectus muscle which subsequently ruptured into the peritoneal cavity, with immediate disappearance of the tumor. The rapidly developing tumors are always accompanied by signs of peritoneal irritation such as belching, nausea, distention, rigidity, and sometimes vomiting. In the slowly developing case the mistake is usually made of diagnosing an intra-abdominal tumor, and if the mass is intramural, it is usually confused with an incarcerated hernia or tumors of the abdominal wall produced by sarcoma, fibroma, desmoid, gumma, tuberculosis or actinomycosis. The most suggestive finding in the slowly developing case is Laffont's sign, namely, discoloration around the umbilicus which has been referred to previously, and was present in Case 3.

Pathology—There was no informative record covering the underlying pathology of this condition. It is significant that Beals, Blanton and Eisen-drath⁷ found eight cases among 140 bronchopneumonias which came to autopsy. They thought the contributing factor was some localization of the infection in the rectus muscle associated with beginning abscess formation followed by rupture and hemorrhage incident to violent coughing. In the pathologic report of Behan's⁸ case there was shown to be an alteration in the muscle fibers, consisting of an exaggerated granulation and hyalin degeneration, suggesting a degenerative process prior to the rupture. The recent hematoma appeared to have been extravasated between these degenerated fibers. The pathologic diagnosis was "chronic myositis." One might ask if the pathologic reaction in this case was contributory to rupture and hemorrhage, or conversely, were the muscle changes above described due to pressure necrosis from the hematoma.

Vascular disturbance followed by hyalin degeneration is the principal pathologic lesion associated with rupture of muscle or vessels within the rectus sheath. This condition seems to occur more frequently within the rectus muscle than in any other single large muscle of the body. Brodel,⁹ in a most scientific treatise on the anatomy of the rectus muscle, covers this problem in great detail. He shows that there are no main arterial trunks in the center of the rectus muscle, but on the other hand, a diffuse capillary bed through which active flow of blood is brought about by muscular contraction. This normal mechanism is often disturbed by pathologic blocking of the capillary beds with resulting hyalin degeneration. This is thought to occur frequently in mild, acute infections, or in healthy individuals without ever being detected. We know that injured or degenerated muscle fibers promptly regenerate, and in a short period of time nothing can be demonstrated either clinically or microscopically. However, regeneration does not take place if there has been a massive injury resulting in a large area of hyalin degeneration of the muscle. Brodel thinks that this condition in a large area, or in numerous small areas scattered throughout the muscle, is conducive to rupture of the muscle fibers or the vessels. The more resistant arteries are less liable to rupture than the frail, thin-walled veins. Any interest whatever on this subject should certainly stimulate one to read Brodel's article.

Anatomy—The principal function of the rectus muscle is regulating the intra-abdominal pressure and aiding the other associated muscles in the act of expiration. It is said that voluntary muscles are capable of contracting down to one-half their length. Brodel quotes the famous artist, Leonardo da Vinci (1452-1519), as stating that the rectus muscle during flexion and extension can stretch and contract as much as nine fingerswidth, which corresponds in the rectus muscle of an athletic youth to about 17 cm. This contraction is controlled by the three transverse tendons which really divide the rectus muscle into four segments, thus providing for segmental contractions in contradistinction to one large central contraction.

The nerve supply comes from the anterior branches of the fifth to the

twelfth thoracic nerve while the vascular system is composed of the terminal branches of the internal mammary commonly spoken of as the superior epigastric artery, while from below, the inferior epigastric ascends to anastomose with the terminal branches of the internal mammary by a very fine capillary plexus. In addition, the central portion of the muscle is further supplied by small arteries coming from the seventh, eighth and ninth intercostals which anastomose with the epigastric plexus. There is a double set of veins accompanying each arterial system, the whole vascular network is situated on the dorsal surface of the rectus muscle.

Incidence of Rupture—The impression is almost universal that spontaneous rupture of the epigastric artery is a very rare occurrence. The following facts taken from the literature controvert this idea. Maydl,¹⁰ in 1882, reviewed the literature from 1809 to 1880, and stated that the condition was accurately described by Hippocrates and Galen. Reference is again made to Leonardo da Vinci's description previous to 1519. Maydl collected 14 cases of spontaneous rupture reported previous to 1880, and Cullen¹¹ is of the opinion that one of the first cases described in this country was by Richardson,¹² in 1857. Wohlgmuth¹³ collected 127 cases up to 1923, 79 of which were below the navel, and 18 below the semilunar fold of Douglas. A study of the literature appearing during the last decade affords 77 articles on this subject, and presents the records of 165 cases for the analysis of the histories, operative findings, and pathologic investigations. There are probably twice this many cases which occurred during this period that have been observed but which were not reported.

Treatment—Early and correct diagnosis, followed by prompt operative evacuation, is the proper treatment. The seriousness of hematoma in the rectus muscle, whether developing spontaneously or otherwise, seems to have been greatly exaggerated, in my opinion, in the articles that have been reviewed. Among the 165 cases reported, there are only three deaths recorded: two from intestinal obstruction reported by Dlugi and del Carril, and one reported by MacLennan³¹ of a man, age 55, in whom the diagnosis of acute intestinal obstruction was made, and nothing found but a hematoma in the middle third of the left rectus muscle. Death occurred on the fourth day, and necropsy showed a hemorrhage to have again recurred, throughout the arterial system there was an advanced degree of arteriosclerosis. The principal danger in the treatment of these cases seems to lie in a mistaken diagnosis, followed by unnecessary procrastination relative to operation. In a large percentage of these delayed operations, infection of the hematoma is superimposed and thus becomes a grave complication. With regard to delayed diagnosis and treatment in these cases, Giese³² reports a most interesting case in which medicolegal aspects assume considerable importance. The patient was a woman, age 86, unhappily located in the home of a couple who were quite unkind to her. She lay abed for two days and died without any physician having been in attendance. Gossip was rife, and the village pastor urged autopsy. The most prominent physical finding was a band of dark

blue discoloration 8 cm wide, on the left side, and extending from the umbilicus to the pubes. Incision yielded dark blood. External violence was charged. Giese was called in to make further examination and found extensive arteriosclerotic changes in various parts of the circulatory system, and also the presence of pneumonia. The verdict was that the extravasation of blood in the muscle occurred as the result of spontaneous seepage, and that death had been due to pneumonia. He does not explicitly mention rupture of the deep epigastric or internal mammary arteries. Considering the frequency of hematoma developing in the rectus muscle and the apparent lack of familiarity with this lesion, it seems pertinent to recall the admonition of Mr. Mailer,³³ who appropriately said that while the abdominal cavity is called Pandora's box, it is highly important that we do not forget "the lid."

CONCLUSIONS

So far, we can only speculate about the causes of hemorrhage into the sheath of the rectus muscle and point to certain predisposing factors. The primary etiologic possibilities may be found either in the muscle itself or in its vessels.

Muscle—Degenerative changes in muscle fibers, predisposing to rupture, are described by several authors, but we should not forget that degenerative changes in muscle fibers can be the consequence of hemorrhage. As to the peculiar localization of this hemorrhage, the nearly unique position of the muscles of the abdominal wall, especially of the rectus, may be pointed out. Except for the small muscle group of the cheek, the muscles of the abdominal wall, and especially the recti, are the only muscles of the human body not supported by an underlying bone. We know that Zenker's degeneration localizes mainly in this muscle, and that this type of degeneration does not only occur in typhoid fever, but also as the result of other infectious conditions. In addition, we know that pregnancy, another of the predisposing factors, leads to both degeneration and regeneration of muscle fibers in the abdominal wall and into an occasional microscopic rupture of the fibers, and that these changes are more pronounced in cases which have had infection during pregnancy. This was proved by Strauss³⁵ in 20 postmortem examinations made during the last month of pregnancy. The peculiar situation of the rectus muscle, infection and pregnancy, may have to be counted among reasons for primary change in the muscle, but to me the other factor—vascular change—seems more important, although any one of the components may play its part.

Vessels—Hemorrhage may arise either from arteries, veins, or from capillaries, and be precipitated by rupture or by diapedesis. When we consider the causes of vascular changes which may have certain connections with the occurrence of this disease, the following may be considered.

(1) *Arteries*—Arteriosclerosis, syphilis, necrosis of the media, the so-called "third disease" of the aorta which leads to spontaneous rupture of this vessel.

(2) *Arteries and Veins*—Infectious changes

(3) *Veins*—Changes in pregnancy

(4) *Capillaries*—Spasm of the arteries leading to anemia, with consecutive damage of the capillaries, which results after release of the spasm, in hemorrhage (diapedesis) from capillaries—one of the mechanisms considered in cerebral apoplexy

Arteriosclerosis, not unlikely, plays its part because the disease in question is likewise one of old age. Syphilis has not been found in these cases. Necrosis of the media is only mentioned incidentally, as we do not know of similar changes occurring in arteries other than the aorta. Infectious changes may play a greater part. They were often present in persons with hemorrhage into the rectus muscle, and in many cases, especially, it was influenza which, according to Stoerk and Eppstein,³⁶ frequently led to vascular changes. In support of the capillary mechanism, we may point to the frequently found ecchymosis, often, however, these may not be differentiated from suggillation, while on the other hand, hypertension is not among the concomitant diseases. Changes in veins, predisposing to hemorrhage, are not uncommon in pregnancy. Varices develop in the abdominal wall as well as in the legs, where only mechanical causes need be considered.

Today, therefore, we are, apparently, not able to determine the definite cause of hemorrhage into the rectus muscle. The possibilities mentioned above may be helpful in further study. We can point to predisposing factors such as old age, pregnancy and infection, and the not infrequently found combination of the latter with one of the former.

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DISCUSSION —DR MONT R REID (Cincinnati, Ohio) I feel that I express the sentiments of this society when I express my personal appreciation to Doctor Payne for his excellent discussion of the subject

The occurrence of this condition in a large charity hospital, such as ours, is frequent enough to bring the subject up for general discussion once every year or so. Yet, as so well expressed by Doctor Payne, the reason for the discussion is that the true condition is not thought of and the patient is operated upon under the assumption that there exists some acute intra-abdominal condition. In a certain sense, then, this condition is analogous to acute mesenteric lymphadenitis or hemorrhage from a graafian follicle, which are so frequently operated upon for acute appendicitis. The analogy rests largely upon the failure of the surgeon to be conscious of, or think of, the occurrence of these conditions. I am quite sure that Doctor Payne's paper will serve to make us conscious of the occurrence of spontaneous apoplexy of the epigastric and internal mammary arteries and, being conscious of this condition, to treat them with fewer instances of erroneous judgment. (I think I am quite safe in saying that a correct diagnosis will lead to an intelligent management of these cases by American surgeons and that a correct diagnosis depends largely upon a consciousness of the incidence of its occurrence.)

That we need look for no specific etiologic cause of this condition seems to me fairly obvious. The epigastric and internal mammary arteries are certainly not immune to those conditions of disease and trauma which make arteries subject to apoplexy in other parts of the body. Besides, the excellent anatomic studies of Cullen and Brodel show why these two vessels may be subjected to inordinate strain during the voluntary and involuntary functions of the body.

The medical profession has long regarded spontaneous arterial hemorrhages as being peculiar to the domain of the central nervous system. Doctor Payne has drawn attention to the fallacy of this assumption. Yet, I would add a word of warning, that they are not peculiar to the central nervous system and the rectus abdominis muscles, they may occur in any part of the body. On several occasions I have detected spontaneous leakage of arteries by hearing a coarse systolic bruit over the course of the peripheral vessels. I wonder if Doctor Payne has ever detected a bruit over hemorrhages into the rectus abdominis muscle?

Very shortly, my friend Dr H. Glenn Bell, of the University of California, will report eight cases of spontaneous hematoma occurring in the rectus muscle. As so aptly expressed to me in a personal communication, he

wonders if minor occurrences of this condition are not frequently overlooked. Among people who normally live sedentary lives but exercise strenuously on Sundays and holidays, he has seen several who complained of severe upper abdominal pain, showed some rigidity of the rectus muscles and a few who showed the signs of an indefinite mass. Yet on most careful study no evidences of intra-abdominal abnormalities could be found. And the patients recovered completely. (It is often said that for every case of pancreatitis which is diagnosed, there must be hundreds which are not recognized, it may be that there are many cases of small unrecognized hemorrhages into the rectus abdominis muscles. Certainly the discussion of this whole problem makes me wonder about several cases which have puzzled me.)

THE REPLACEMENT OF SODIUM CHLORIDE IN SURGICAL PATIENTS*

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THE IMPORTANCE of replacing the sodium chloride and water which may be lost from the body by such abnormal ways as vomiting, gastroduodenal suction, diarrhea, drainage from biliary and intestinal fistulae has been emphasized since the investigations of O'Shaughnessy,¹ Hartwell and Hoguet,² MacCallum, Lintz, Vermilye, Leggett, and Boas,³ Haden and Orr,^{4, 5, 6, 7, 8} Gamble and Ross,⁹ and many others,^{10, 11, 12} showed the value of such therapy. In practice, when a salt deficiency exists the amount of sodium chloride given has been largely empiric, one to five liters of saline solution being administered and the sodium chloride restoration followed by blood chemistry studies. This method has at least two faults. If the sodium chloride needs of the patient have been underestimated, valuable time is lost in restoring the body chemistry to normal, and secondly, if an excessive amount of salt is given, the error will not be shown by the blood chemistry studies and the patient may develop edema.^{13, 14, 15, 16, 17, 18} The purpose of this paper is to present briefly‡ data leading to simple accurate rules for (1) The maintenance of a normal sodium chloride concentration in patients losing sodium chloride while under observation, and (2) the restoration of sodium chloride in patients whose sodium chloride concentration is below normal when first examined.

The Maintenance of a Normal Sodium Chloride§ Concentration—In actual surgical practice the problem of maintaining a normal sodium chloride level deals mainly with the patient who, while in the hospital, is losing important amounts of water and sodium chloride through loss of gastro-intestinal secretions. In 1937, Dick, Maddock and Coller¹⁹ pointed out that the concentration of sodium chloride in these secretions is almost always less than the concentration of sodium chloride in physiologic saline or Ringer's solution, and they suggested that if one replaced the secretion loss by an equal volume of these solutions, a satisfactory water and salt balance should be maintained.

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‡ A more complete presentation of sodium chloride metabolism in surgical patients will be published subsequently.

§ Throughout the study only the chloride ion was measured and, as is customary, its value was expressed in terms of sodium chloride.

To determine the value of this volume-for-volume rule a series of patients who were losing alimentary tract secretions were studied in the following manner. Immediately after operation each patient was weighed on a special scale, a blood specimen was taken for the determination of the plasma chlorides, a Levine tube was inserted into the stomach and gastroduodenal suction was instituted. Nothing was given by mouth and the water requirements for the day were provided for by the intravenous administration of 5 per cent glucose in distilled water. On the following morning the patient was weighed, the 24-hour specimens of urine and alimentary tract drainage were measured and their chloride content determined, and blood was again taken for a plasma chloride determination. A volume of physiologic saline or Ringer's solution equal to the volume of drainage for the previous 24 hours was then given intravenously, and in addition sufficient 5 per cent glucose in distilled water to provide for the water needs of the body. For the several days that this procedure was carried out no stools were passed. The salt losses through the skin were not determined but in no case was there profuse sweating. The

TABLE I

REPLACEMENT OF UPPER GASTRO INTESTINAL SECRETION LOSSES WITH EQUAL VOLUMES OF
PHYSIOLOGIC SALINE SOLUTION

		1 Liter \approx 8.5 Gm NaCl								
		Secretions Lost					Salt Given			
Patient	24 Hours Ending	Body Weight Kg	G I Tract Cc	Bile T-Tube Cc	Total		Phys Saline Cc	Salt Content Gm	Plasma Chlorides Mg NaCl/ 100 Cc	NaCl in Urine Gm
					Volume Cc	NaCl Gm				
E K	2-18	—	—	—	—	—	—	—	556	—
	2-19	49.36	320	400	720	2.94	0	0	528	2.45
	2-20	47.86	850	290	1,140	7.50	708	6.03	528	1.10
	2-21	48.26	0	290	290	1.75	1,165	9.90	540	1.06
	2-22	47.67	0	250	250	1.49	287	2.44	540	1.11
	2-23	47.44	0	250	250	1.01	478	4.06	564	1.26
			1,170	1,480	2,650	14.69	2,638	22.43		6.98
E M	3-9	58.01	—	—	—	—	—	—	582	—
	3-10	59.06	900	0	900	6.46	0	0	490	1.21
	3-11	57.25	840	0	840	4.94	865	7.35	492	1.65
	3-12	56.85	920	0	920	5.69	835	7.01	505	1.51
	3-13	56.30	1,020	0	1,020	5.30	922	7.84	490	0.70
	3-14	56.50	0	0	0	0	1,030	8.76	513	0.80
			3,680	0	3,680	22.39	3,652	30.06		5.87
M M	2-21	42.01	—	—	—	—	—	—	571	—
	2-22	42.62	220	0	220	0.56	990*	5.86	533	6.85
	2-23	41.32	350	0	350	2.23	243	2.07	540	1.42
	2-24	41.65	390	0	390	2.45	354	3.01	541	1.11
	2-25	40.26	0	0	0	0	385	3.27	545	1.53
			960	0	960	5.24	1,872	14.21		10.91
M A	4-5	54.46	—	—	—	—	—	—	568	—
	4-6	—	490	160	650	4.12	0	0	490	2.17
	4-7	53.26	780	240	1,020	6.40	669	5.69	500	3.12
	4-8	51.29	910	230	1,140	7.63	1,010	8.50	512	1.59
	4-9	50.87	0	215	215	1.08	1,150	9.78	535	0.98
	4-10	50.92	0	220	220	1.14	393	3.34	545	0.76
			2,180	1,065	3,245	20.37	3,222	27.40		8.62

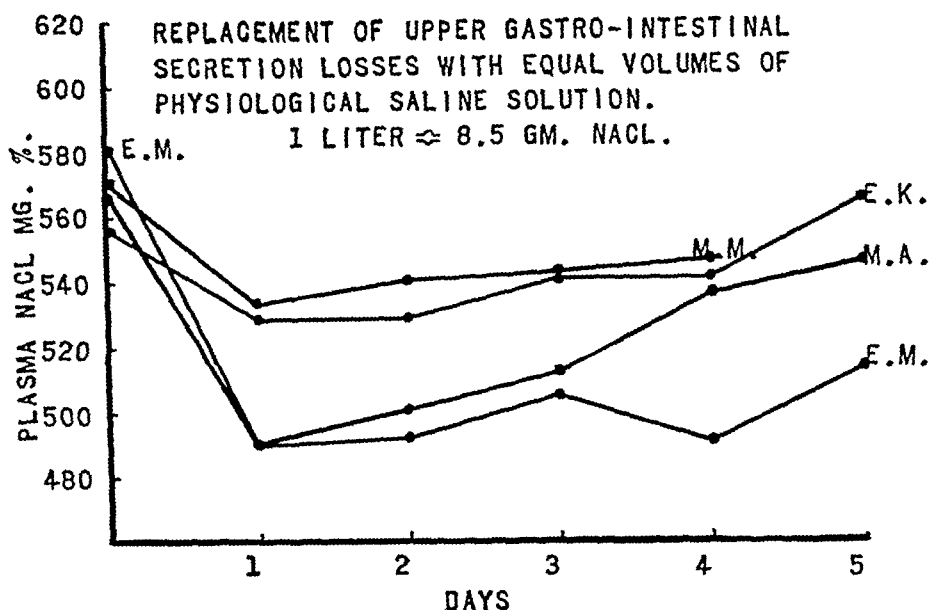
* 465 cc physiologic saline solution and 425 cc of blood

REPLACEMENT OF SODIUM CHLORIDE

patients did not gain in weight, therefore it was assumed that an excessive amount of salt leading to the development of water retention had not been given

In Table I the data from the patients having their sodium chloride losses replaced with physiologic saline solution are given. The resulting plasma chloride levels are shown graphically in Chart I. Three of the patients (M. M., E. K., and M. A.) maintained a satisfactory plasma chloride level and excreted more than 1 Gm. of sodium chloride in the urine daily. Although the plasma chlorides of the fourth case, E. M., did not fall to a seriously low

CHART I



level, nevertheless, they were definitely below normal. This may be a failure of the volume-for-volume rule, or it may be an example of a patient whose plasma chloride level cannot be brought up to normal.*

In Table II are given the data from the patients whose gastroduodenal secretion losses were replaced by equal volumes of a Ringer's solution containing the equivalent of 7.55 Gm. of sodium chloride per liter†. It will be noted that all of the cases studied (W. W., J. B., A. G., and M. L.) maintained a plasma chloride level above 500 mg. NaCl per 100 cc., but in each the daily urinary excretion of sodium chloride fell below 1 Gm., indicating what we at this time, believe to be an inadequate excess of salt.

In all except one of the cases of Charts I and II (W. W. of Chart II) there is a definite fall in the plasma chloride concentration during the first 24 hours of the gastro-intestinal fluid drainage, no salt being given during this time. A fairly constant plasma chloride level is thereafter maintained by the volume-for-volume replacement, with a tendency in most cases for the

* This inability to raise the plasma chloride level to normal has been observed in a number of patients.

† Ringer's solution, as made by different laboratories, varies in its composition.

TABLE II

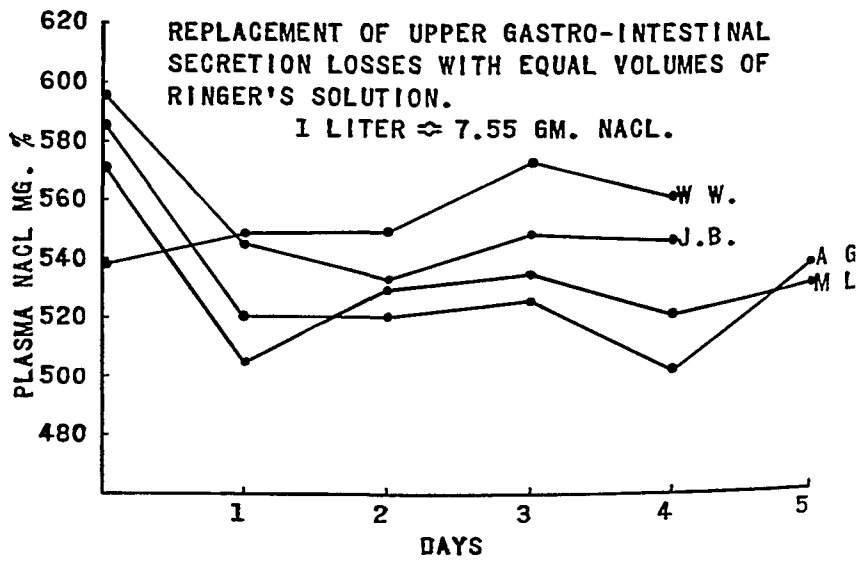
REPLACEMENT OF UPPER GASTRO-INTESTINAL SECRETION LOSSES WITH EQUAL VOLUMES OF RINGER'S SOLUTION

1 Liter \approx 7.55 Gm NaCl

Patient	24 Hours Ending	Body Weight Kg	Secretions Lost				Salt Given		Plasma Chlorides Mg NaCl/ 100 Cc	NaCl in Urine Gm
			G I Tract Cc	Bile T Tube Cc	Total		Ringer's Solution Cc	Salt Content Gm		
					Volume Cc	NaCl Gm				
W W	I-4	81.77	—	—	—	—	—	—	538	—
	I-5	80.00	960	1,000	1,960	9.97	0	0	548	0.73
	I-6	78.82	290	810	1,100	6.88	2,035	15.36	549	0.54
	I-7	77.81	0	315	315	20.3	1,133	8.55	573	2.10
	I-8	76.96	0	0	0	0	318	2.30	561	0.35
			1,250	2,125	3,375	18.88	3,486	26.21		3.72
J B	I-10	73.00	—	—	—	—	—	—	596	—
	I-11	74.50	480	0	480	2.65	0	0	545	3.86
	I-12	73.23	505	0	505	3.30	485	3.66	533	5.19
	I-13	72.33	280	0	280	1.57	522	3.81	548	0.48
	I-14	72.07	0	0	0	0	318	2.40	546	0.32
			1,265	0	1,265	7.52	1,325	9.87		9.85
A G	I-10	51.64	—	—	—	—	—	—	586	—
	I-11	—	320	190	510	3.51	800*	4.80	520	1.61
	I-12	49.65	775	180	955	7.18	517	3.90	520	1.02
	I-13	48.78	855	130	985	7.49	945	7.13	526	0.49
	I-14	48.25	860	70	930	5.95	963	7.27	502	0.34
	I-15	49.38	0	150	150	0.88	956	7.22	538	0.27
			2,810	720	3,530	25.01	4,181	30.32		3.13
M L	I-24	52.91	—	—	—	—	—	—	571	—
	I-25	52.15	570	290	860	5.60	0	0	505	4.82
	I-26	49.85	540	340	880	4.62	835	6.30	530	0.51
	I-27	49.03	520	250	770	4.41	900	6.79	535	0.17
	I-28	49.76	0	300	300	1.26	787	5.93	521	0.06
	I-29	49.06	0	260	260	1.57	317	2.39	531	0.13
			1,630	1,440	3,070	17.46	2,839	21.41		5.69

* 300 cc of physiologic saline solution and 500 cc of blood

CHART II



REPLACEMENT OF SODIUM CHLORIDE

level to rise on the last day of the study. In an attempt to eliminate this initial drop and thus to maintain the plasma chlorides at a higher level, a series of four patients were given about 1,000 cc of physiologic saline solution during the first 24 hours of the study. Then, as in the previous cases, the gastro-intestinal secretion losses were replaced volume-for-volume with physiologic saline solution.

TABLE III

REPLACEMENT OF UPPER GASTRO-INTESTINAL SECRETION LOSSES WITH EQUAL VOLUMES OF
PHYSIOLOGIC SALINE SOLUTION PLUS 1,000 CC PHYSIOLOGIC SALINE SOLUTION DURING
THE FIRST 24 HOURS

1 Liter \approx 85 Gm NaCl

Patient	24 Hours Ending	Body Weight Kg	Secretions Lost				Salt Given		Plasma Chlorides Mg NaCl/ 100 Cc	NaCl in Urine Gm
			G I Tract Cc	Bile T-Tube Cc	Total		Phys Saline Cc	Salt Content Gm		
					Volume Cc	NaCl Gm				
I D	3-16	—	—	—	—	—	—	—	591	—
	3-17	66 20	120	0	120	0 80	1,050	8 91	561	3 77
	3-18	65 15	110	0	110	0 76	120	1 02	568	1 01
	3-19	63 62	335	0	335	2 27	110	0 93	578	1 33
	3-20	64 03	0	0	0	0	342	2 91	584	0 50
			565	0	565	3 83	1,622	13 77		6 61
E R	3-19	46 56	—	—	—	—	—	—	559	—
	3-20	47 29	630	0	630	4 50	1,010	8 60	563	0 36
	3-21	45 30	1,020	0	1,020	7 53	640	5 36	563	0 46
	3-22	44 11	1,890	0	1,890	12 36	1,020	8 65	553	0 13
	3-23	43 21	2,500	0	2,500	19 28	1,920	16 32	530	0 09
	3-24	43 17	3,000	0	3,000	20 76	2,510	21 33	528	0 14
	3-25	42 54	2,330	0	2,330	15 38	3,080	26 20	611	0 41
			11,370	0	11,370	79 81	10,170	86 46		1 59
L W	3-22	56 09	—	—	—	—	—	—	579	—
	3-23	59 22	320	0	320	1 96	1,060	9 01	543	3 08
	3-24	57 09	310	0	310	1 82	325	2 76	546	9 02
	3-25	54 45	600	0	600	4 01	314	2 67	594	1 97
	3-26	55 46	0	0	0	0	582	4 91	592	0 64
			1,230	0	1,230	7 79	2,281	19 35		14 71
M L	4-12	40 08	—	—	—	—	—	—	602	—
	4-13	40 94	260	220	480	2 87	1,600 ^b	11 41	578	1 33
	4-14	39 06	250	390	640	3 69	486	4 13	568	4 81
	4-15	38 67	0	370	370	2 07	632	5 37	569	1 59
	4-16	37 64	0	390	390	2 17	722	6 14	558	2 12
			510	1,370	1,880	10 80	3,440	17 05		9 85

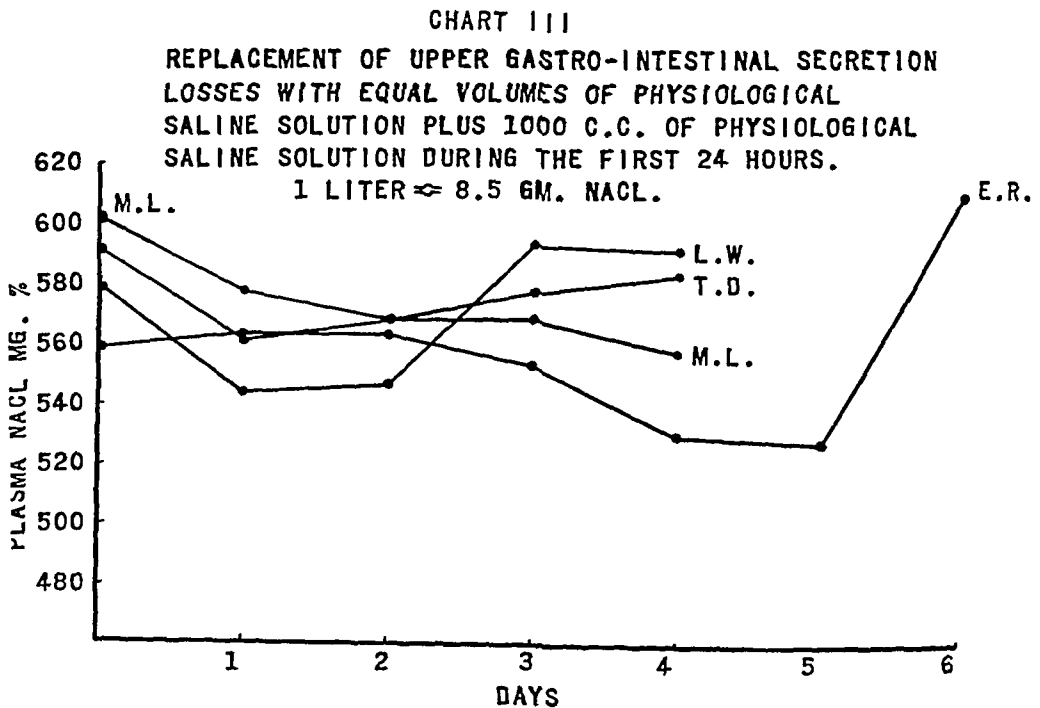
* 1,050 cc of physiologic saline solution and 550 cc of blood

The data from this study are shown in Table III, and graphically presented in Chart III. It will be seen that three of the four cases showed an initial drop in the plasma chloride level in spite of the administration of more than sufficient saline solution to balance the abnormal losses during this period. However, the fall was not as marked as in the cases presented in Tables I and II in which no saline solution was given during the first 24-hour period. Also, the plasma chlorides were maintained at a higher level for the remaining days of the study than was the case for the previous patients.

The maintenance of a satisfactory sodium chloride level in patients losing

significant amounts of gastro-intestinal tract secretions seems to be possible by following the volume-for-volume replacement rule plus the administration of about one liter of physiologic saline solution during the first 24 hours. This latter procedure was added to decrease the initial fall in plasma chlorides which so frequently occurs.

The Restoration of Sodium Chloride—The idea of putting the sodium chloride needs of patients on a quantitative basis is not new. In 1923, Haden and Oll⁷ suggested that in well advanced intestinal obstruction the patient should be given an initial dose of 1 Gm. of sodium chloride per kg. of body weight. Recently, Falconer and Lyall²⁰ made a further advance in accurate



sodium chloride therapy. They gave known amounts of salt to patients with hypochloremia and determined the resulting rise in the plasma chloride level. From their studies they concluded that "in hypochloremia about 20 grammes (from 15 to 30 grammes) of salt are required on the average to raise the plasma chloride by 100 mg. per 100 cc."

Early in our²¹ investigation of the salt requirements of surgical patients two simple but fundamental principles became apparent. First, it seemed obvious that the salt needs of a 20 Kg. child must be quite different from those of an adult weighing three times that much. Second, it was thought that if one could determine what percentage of the body salt had been lost, it should be possible to calculate accurately the amount of salt that must be given to restore the body chlorides to normal provided the normal salt content of the body is known.

Various estimations of the total chlorine content of the body have been made. Sherman²² stated the amount to be 0.15 per cent of the body weight.

REPLACEMENT OF SODIUM CHLORIDE

Expressed as sodium chloride, this amounts to 0.248 per cent of the body weight. On this basis there are 148.8 Gm of salt in a 60 Kg individual and 49.6 Gm in a 20 Kg child. The importance of body weight in calculations of salt requirements is thus apparent.

As an index of the state of the total body sodium chloride concentration, the value of the plasma chloride level was considered. It has been shown by White and Bridge²¹ that a fall in tissue chlorides is directly proportional to the fall in plasma chloride concentration. From this we assume that the plasma chloride concentration can be used as an index of the chloride concentration throughout the body. On this basis, if the plasma chlorides are 20 per cent below normal it is reasonable to consider that about 20 per cent of the body chlorides have been lost. In the previous paragraph are given data that can be used for calculating the total sodium chloride content of the body. With these data and the plasma chloride level one should be able to calculate the grams of salt necessary to be given to a patient with hypochloremia to restore the chlorides to normal, as follows:

(1) Per cent of body salt lost

$$= \frac{\text{normal plasma chlorides} - \text{actual plasma chlorides}}{\text{normal plasma chlorides}} \times 100$$

(2) Total NaCl content of body = 0.248 per cent of body weight (Gm)

From (1) and (2)

(3) Number of grams of NaCl needed to restore body chlorides to normal

$$\begin{aligned} &= \text{per cent of body salt lost} \times \text{total NaCl content of body} \\ &= \frac{\text{normal plasma chlorides} - \text{actual plasma chlorides}}{\text{normal plasma chlorides}} \times 100 \times \\ &\quad 0.248 \text{ per cent of body weight (Gm)} \\ &= \frac{560 - \text{actual plasma chlorides}}{560} \times 0.00248 \times \text{body wt (Gm)} \end{aligned}$$

Applying the last equation to the example of a 60 Kg patient admitted to the hospital with a plasma chloride level of 410 mg NaCl per 100 cc, the formula shows the amount of sodium chloride needed to restore the plasma chloride level to 560 mg per cent, *i.e.*, $\frac{560 - 410}{560} \times 0.00248 \times 60,000 = 39.9 \text{ Gm}$

In order to determine the practical value of this formula, it was applied to a series of individuals with hypochloremia. This group included instances of pyloric and intestinal obstruction, rectal polyp with profuse rectal discharge, paralytic ileus and patients who had been on gastroduodenal suction without accurate replacement of the drainage loss. The patients were given an amount of salt calculated as necessary to restore the plasma chlorides to 560 mg NaCl per 100 cc. The salt was given intravenously in the form of

The normal plasma chloride level varies from 560 to 630 mg per 100 cc. The lower limit was selected for the calculations because many sick patients will not attain a higher level.

physiologic saline or Ringer's solution at the rate of about 500 cc per hour. During the period of study, 24-hour specimens of urine were collected and the chlorine content determined. If the patient was losing chlorides through some abnormal source during the period of correction of the hypochloremia, these losses were also collected and the salt content determined. These losses in most instances were replaced by the volume-for-volume rule.

TABLE IV

RESTORATION OF BODY CHLORIDES

The formula and clinical calculations are on the basis of a normal plasma chloride concentration of 560 mg NaCl/100 cc

Patient	Body Weight Kg	Initial Plasma Chlo-rides	Initial Plasma CO Comb Power	NaCl Given Gm	NaCl Lost During Restoration				NaCl Retnd Gm	For- mula Cal- cula- tion Gm	Final Plasma Chlo-rides	Final Plasma CO Comb Power	Final Clin- cu- la- tion Gm
		Mg	Vol		Urine Gm	Tract Gm	Stool Gm	Total Gm			Mg	Vol	
		NaCl/100 Cc	%								NaCl/100 Cc	%	
O M	63.3	404	57.6	55.8	7.7	7.3	0	15.0	40.8	43.7	559	52.0	49.6
B S	39.0	449	53.6	28.4	9.2	1.2	0	10.4	18.0	19.2	493	67.1	21.6
J C	65.5	479	45.7	27.5	2.6	1.4	0	4.0	23.5	23.4	586	44.7	26.5
D C	60.4	513	59.8	15.8	1.3	0	0	1.3	14.5	12.6	564	53.9	14.2
D E	58.1	345	100.0	100.6	6.2	38.1	?	44.3	56.3	55.3	606	73.0	62.5
L A D	62.0	372	75.0	70.1	14.9	5.5	0	20.4	49.7	51.6	566	60.0	58.3
C K	48.9	356	48.0	56.8	0.7	1.1	17.9	19.7	37.1	44.1	528	49.8	49.8
S L	21.8	479	—	8.7	0.9	0	0.8	1.7	7.0	7.8	536	—	8.8
L B D	54.0	464	—	25.7	5.4	0.3	0	5.7	20.0	22.9	554	—	25.9
B M	34.0	437	—	21.3	0.2	0	0	0.2	21.1	18.5	513	—	20.9
T J	72.7	427	59.9	40.6	0.0	0	0	0.0	40.6	42.7	564	48.0	48.3
W P	67.7	436	57.3	33.7	1.5	0	0	1.5	32.2	37.1	543	58.3	42.0
J W	59.8	447	61.4	26.2	1.1	0	0	1.1	25.1	29.7	546	58.9	33.8
S T	73.2	436	67.3	42.8	0.5	0	0	0.5	42.3	39.8	554	56.3	45.4
H A	76.9	454	49.5	38.2	0.7	0	0	0.7	37.5	35.6	545	60.7	40.8

The data from this study are shown in Table IV. The close correlation between the amount of salt retained and the amount needed as determined by the formula calculation indicates that the principles of salt replacement previously discussed are sound. In most instances the plasma chloride level determined from 12 to 36 hours after the completion of the saline administration was fairly close to 560 mg NaCl per 100 cc.

Because of important illustrative points, several cases deserve special comment.

Patient B S attained a final plasma chloride level of only 493 mg per 100 cc. However, this seemed to be the highest level the patient could reach at the time, since she excreted 9.2 Gm of sodium chloride in the urine and further administration of salt failed to raise the plasma chloride level significantly.

Patient C K was moribund when first seen. She had a large rectal polyp associated with frequent watery stools and a profuse rectal discharge, the salt content of which was found to be 5.5 Gm per liter. Before half of the necessary salt was administered she was awake, and within 24 hours was sitting up in bed and mentally alert. One of the characteristic findings in patients recovering from hypochloremia is a definite euphoria as the plasma chlorides

approach normal. The final plasma chloride level in this patient was only 528 mg per 100 cc, but it will be noted that the actual salt retention fell 7 Gm short of the calculated need. This was due to the fact that the patient was losing more salt in the rectal discharge than had been anticipated. The rectal polyp was removed and the patient left the hospital cured. If her moribund state had not been recognized as due to hypochloremia, an operation would never have been possible.

Patient L. A. D. illustrates another instructive point. She was a female, age 82, with a strangulated femoral hernia. Her calculated salt requirement was 51.7 Gm but by mistake she was given 70.1 Gm. Of the excess 19.4 Gm, 5.5 Gm were lost in gastroduodenal drainage and 14.9 Gm were excreted in the urine. In general, small excesses of salt are readily eliminated by the kidneys, but, as others have pointed out, large excesses in sick patients tend to cause edema.

Although the formula was found to be accurate, it is cumbersome, and a search was made for a simpler calculation. Using the formula as a basis, several simple approximations were found, the following being considered the most satisfactory. For each 100 mg per cent that the plasma chlorides need to be raised to reach the normal of 560 mg NaCl per 100 cc, the patient should be given 0.5 Gm of sodium chloride per Kg of body weight.* Example: For a 60 Kg patient with a plasma chloride concentration of 410 mg per cent, the amount of sodium chloride needed is $15 \times 0.5 \times 60 = 450$ Gm. The figures in the last column in Table IV were calculated on this basis and when compared to the formula calculation they show the adequacy of this simple clinical rule. By its use a slight excess of salt will be given, a desirable feature, without danger.

Discussion—The clinical syndrome presented by patients with depleted body chlorides is worthy of special comment. They are definitely depressed. There is marked lassitude, weakness, and fatigue. The patient's mentality is dulled, and, in the most severe cases, there may even be stupor and coma. The gastro-intestinal symptoms include, first, a dulling of the sense of taste,²⁴ followed by anorexia, nausea, and vomiting. Muscular cramps also often

* For those who are accustomed to expressing body weight in terms of pounds rather than kilograms, the following rule, which provides for slightly less salt than the clinical calculation, has been formulated. For each 100 mg per cent that the plasma chlorides need to be raised, the patient should be given 0.2 Gm of sodium chloride per pound of body weight.

In some laboratories whole blood chlorides rather than plasma chlorides are determined. Using 450 mg NaCl per 100 cc as the normal for whole blood, the formula calculation would be

Gm NaCl needed

$$= \frac{450 - \text{actual blood chlorides}}{450} \times 0.248 \text{ per cent of body weight (Gm)}$$

A clinical rule derived from this formula is as follows. For each 100 mg per cent that the whole blood chlorides need to be raised, the patient should be given 0.6 Gm of sodium chloride per Kg, or 0.25 Gm per pound of body weight.

occur. Dehydration, characterized by a dry tongue, sunken eyes, and dry inelastic skin almost invariably accompanies hypochloremia. A low pulse pressure has also been observed, two of our patients presented the clinical picture of shock. Alkalosis with slow respirations and tetany, or inorganic acidosis with deep respirations, may or may not be associated with the chloride depletion.

In the consideration of sodium chloride maintenance and restoration we have dealt with the chloride ion only because, for clinical purposes, its determination is easier than that of sodium. Indirect information concerning the plasma sodium concentration derived from the estimation of the carbon dioxide combining power is always relative to the chloride concentration at that time. For example, gastroduodenal drainage usually contains about equivalent amounts of sodium and chlorine. The loss of a significant volume of these secretions will deplete the body of about equal amounts of sodium and of chlorine, and while the plasma chloride concentration will be definitely lowered, the carbon dioxide combining power will usually be within normal limits. By our use of the plasma chloride determination no implication was intended that chloride is more important than sodium. Undoubtedly the sodium ion is as important, if not more important, than the chloride ion. This was stressed by Gamble and Ross.⁹ In actual surgical practice, the correction of the chloride depletion with sodium chloride also corrects the sodium deficiency which always exists in some degree when gastro-intestinal secretions have been lost. This was emphasized by Gamble,²⁵ who pointed out that sodium chloride given with an abundance of water will correct either alkalosis or inorganic acidosis, the kidneys excreting the unnecessary ion.

It is important to remember that salt is always lost from the body together with water in concentrations which are always less than that of physiologic saline solution. It is apparent, therefore, that salt used for the restoration of body chlorides should be given in isotonic or hypotonic solutions. Hypertonic solutions have the disadvantages that they further dehydrate the patient, and they tend to produce inaccuracies in salt administration by causing salt losses in diarrheal stools. In this study it has been found that physiologic saline or Ringer's solution, given at the rate of 400 to 500 cc per hour, is retained and corrects sodium chloride deficiency and dehydration. The additional water needed for the daily output of urine and vaporization should be given in the form of 5 per cent glucose in distilled water.

SUMMARY AND CONCLUSIONS

The replacement of sodium chloride lost from the body by vomiting, gastroduodenal drainage, drainage from biliary and intestinal fistulae, diarrhea, wound drainage, and occasionally profuse sweating is a practical problem frequently encountered by the surgeon. Serious depletion of the body sodium chloride will lead to death unless the condition is corrected.

To maintain the normal sodium chloride content of the body in surgical patients losing sodium chloride abnormally while under observation, the fol-

lowing procedure was found to be satisfactory Administer a volume of physiologic saline solution equal to the volume of the abnormal fluid losses This procedure has a very practical application when intubing, gastroduodenal suction is employed In addition to the volume-for-volume rule, in this instance it has been found advisable to give 1,000 cc of physiologic saline solution during the first day of the drainage period in order to lessen the initial fall in plasma chlorides which commonly occurs

To restore to normal the sodium chloride content of a patient depleted of these substances, the following clinical rule was found to be effective For each 100 mg per cent that the plasma chlorides need to be raised to reach the normal (560 mg NaCl per 100 cc) the patient should be given 0.5 Gm of sodium chloride per Kg of body weight

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DISCUSSION —DR THOMAS G ORR (Kansas City, Kans) In 1925, Gamble and Ross made the statement that "sodium chloride is the only one of a long list of salts containing both of the ions specifically required for plasma repair" Potassium chloride, calcium chloride, magnesium chloride and ammonium chloride have no value in plasma repair

The treatment of patients with sodium chloride is a logical and simple type of chemotherapy, being merely a substitution of a body chemical lost by disease To supply sodium chloride in hypochloremia is comparable to the transfusion of blood for anemia and is just as essential to life

In addition to the physiologic properties of sodium chloride already mentioned, it may play a rôle in growth, bactericidal power of the blood and maintenance of bowel tone The prompt response of peristalsis when sodium chloride is given to some patients with distention and hypochloremia leads to the belief that the chloride balance affects the intestinal tone

We have found, in some recent experiments upon dogs, that sodium chloride is absorbed from the stomach and upper intestine when the jejunum obstructed 25 cm below the ligament of Treitz Animals permitted to drink 0.6 per cent sodium chloride live twice as long as animals drinking water The blood chlorides show relatively little change in the group receiving the salt as compared to those drinking water

How much water and how much salt to give a sick patient has long been a practical problem Before the work of Collier and his associates the needs the patient were estimated by his clinical appearance and the estimation the blood chlorides If this is done with understanding, it is quite satisfactory However, one only needs to observe his own patients and particularly those of his confieres who are not familiar with chloride metabolism to realize the gross inaccuracies of such treatment and the desirability of having a quantitative estimate upon which treatment with water and salt may be based Everyone who has been interested in sodium chloride therapy in its clinical and experimental aspects realizes the wide margin of safety of this treatment It is equally well known that too much or too little sodium chloride will cause definite symptoms which mean serious consequences unless corrected The normal patient or experimental animal will tolerate enormous quantities of sodium chloride without apparent harm, but the sick patient, particularly those who have undergone a starvation period with a reduction

in blood protein, frequently develops an edema which may involve the parenchymatous organs

From a practical standpoint the method of estimating the quantity of salt needed by equation seems much preferable to measuring the fluids lost and replacing them with the same quantity of physiologic sodium chloride solution. Part of the value of the gastric suction treatment is the pleasure and comfort afforded the patient by drinking water. Any liquid swallowed would upset the balance of measured gastric intake and output. The practical value to the average surgeon of Coller's quantitative method of administering sodium chloride is quite obvious.

DR. FREDERICK A. COLLER (closing). We all realize the importance of restoring the biochemical balance of the sick patient. The present communication is another effort on our part to furnish the clinician with practical working quantitative methods for accomplishing this. Previously, we have reported other studies showing that water losses are the measurable losses from the body, plus an average loss of two liters from the skin and lungs, that enables one to maintain water balance with sufficient accuracy. We have reported our observations showing that the clinical picture of dehydration was produced by the loss of 6 per cent of the body weight in water, and have emphasized the need of replacing fluid and electrolyte losses by the proper fluid, emphasizing the danger of employing saline solutions routinely as a vehicle.

In the present communication we hope to have demonstrated a sound method for replacing sodium chloride losses in an accurate way, simple enough to have an easy clinical application. Hypochloremia is not uncommonly seen in the sick patients in the surgical wards. The symptoms and signs of hypochloremia are not infrequently attributed to the disease causing the loss of body chlorides and often are not recognized as being due primarily to the altered body chemistry. The findings most commonly encountered in this condition are marked lassitude, weakness and a sense of great fatigue. There are dulling of the mentality, drowsiness verging toward stupor and coma, dulling of the sense of taste, anorexia, nausea and vomiting—with occasionally muscle cramps. There are signs of dehydration—dry tongue, sunken eyes, dry inelastic skin and a low pulse pressure. The final proof of the diagnosis rests with the determination of the plasma chloride concentration. Not infrequently alkalosis or inorganic acidosis is also present, alkalosis if the chloride losses are from the stomach. The carbon dioxide combining power as determined shows the acid-base balance and may show alkalosis or inorganic acidosis or be normal with a marked hypochloremia.

In actual surgical practice, the correction of the chloride depletion with sodium chloride almost invariably corrects any disturbance in the acid-base balance. This has been emphasized by Gamble, who pointed out that sodium chloride given with an abundance of water will correct either alkalosis or an inorganic acidosis, the kidneys excreting the unnecessary ion. It is important to remember that salt is always lost from the body together with water in concentrations always less than that of physiologic saline. It is apparent, therefore, that salt used for the restoration of body chlorides should be given in isotonic or hypotonic solutions. In this study, it has been demonstrated that physiologic saline or Ringer's solution given intravenously at the rate of 400 to 500 cc per hour is retained, and corrects both sodium chloride deficiency and dehydration. The additional water needed for the daily out-

put of urine and for vaporization should be given in the form of 5 per cent glucose in distilled water

One should emphasize that death may occur when the plasma chlorides fall to approximately half the normal level. Symptoms are usually present when the plasma chlorides fall to a point below 500 mg /100 cc, and that they become serious when they get as low as 400 mg /100 cc. We have been on the lookout for this condition, nevertheless we have nearly lost four patients this year from hypochloremia. In every patient who has lost, or is losing fluid from any part of the gastro-intestinal tract, one must keep careful check of the plasma chlorides, and if they are low they can be replaced with sufficient accuracy by using the formula presented

BRIEF COMMUNICATION AND CASE REPORT

ACUTE CHOLECYSTITIS IN A *BACILLUS TYPHOSUS* CARRIER

(CHOLECYSTOSTOMY—CHOLECYSTECTOMY—CHOLEDOCHOTOMY)

CONSTANTINE J. MACGUIRE, JR., M.D.

NEW YORK

Case Report—Hosp No 78536 A B, female, age 40, was admitted to the First Medical Division, Bellevue Hospital, February 22, 1937, with a positive blood culture of *Bacillus typhosus* and a typical clinical picture. March 1, 1937, stools were still positive for typhoid bacilli. On March 31, stools were negative for typhoid bacilli. The Board of Health examined them on the 1st, 2nd, 9th and 17th of April, 1937, all of which were negative for typhoid bacilli. The patient was discharged April 20, 1937, apparently cured of an ordinary attack of typhoid fever. She complained only of a slight pain in the right upper quadrant.

She was readmitted April 29, 1937, with a temperature of 104° F, pulse 120, blood count 10,300, polys 81 per cent, three plus bile in the urine and marked jaundice of six days' duration, clay colored stools and an icteric index of 72. Previous to readmission she had developed severe pain in the right upper quadrant, fever and chills but no pruritus. Tongue was dry, liver palpable two fingersbreadth below the costal arch, the spleen was palpable and hard, van den Bergh direct, immediate—indirect positive. During the next three days she was very toxic with a temperature as high as 105½° F. On May 4, temperature and pulse commenced to subside. Bile reappeared in the stools and the icterus diminished. Blood culture negative for typhoid and paratyphoid. On May 6, stools were found positive for typhoid bacilli. Duodenal drainage was instituted and about five cubic centimeters of brown bile aspirated 15 minutes after the administration of magnesium sulphate. This showed *Bacillus typhosus* on culture. The icteric index was now 16. Temperature, sepsis and jaundice decreased progressively until May 12, 14 days after admission, when her pulse and temperature were practically normal. The abdomen had become soft except for some spasm in the right upper quadrant, and local tenderness. On May 15, the acute process apparently lighted up again—temperature 104° F, pulse 120 both of which subsided somewhat during the next few days but the white blood count of over 20,000, persisted with polys 93 per cent. There was persistent abdominal rigidity, more marked in the R U Q, but the jaundice had not recurred.

Operation—May 19, 1937. The gallbladder showed evidence of an old chronic cholecystitis. It was shrunken and fibrotic and was the seat of an acute suppurative process. It was buried in a mass of adhesions which involved the stomach and transverse colon and contained many large, hard stones and a moderate amount of very yellow, slimy pus. No attempt was made to detach the adhesions but the main part of the gallbladder was removed leaving the cystic duct and a small pouch of the viscus itself. The stones were removed and the pouch packed with gauze, the peritoneal cavity being walled-off by a rubber dam. The pus from the gallbladder showed a pure culture of *Bacillus typhosus*. She had a smooth convalescence, but there remained a persistent biliary fistula which discharged material which continued to show *Bacillus typhosus* on

* Presented before the New York Surgical Society October 27, 1937. Submitted for publication January 4, 1938.

culture The stools also remained positive for *Bacillus typhosus* She had repeated blood transfusions both before and after the operation

Because of the persistence of the *Bacillus typhosus* in the stools, she was again operated upon July 7, 1937 The remnants of the gallbladder were buried in a mass of dense adhesions through which ran a fistulous tract which discharged bile After this had been removed, it was found there were many stones in both the common and right hepatic ducts The common duct was opened and the stones removed The right hepatic duct was then evacuated of its calculi and flushed out with saline A catheter was introduced into the common duct and advanced up into the right hepatic duct Convalescence was unusually smooth The first examination of the stool was made six days postoperative and showed no typhoid bacilli, but the discharge from the abdominal wound continued to show a culture of *Bacillus typhosus* until July 27 On August 6, culture from the wound showed only *Staphylococcus aureus* On August 11, the wound showed only superficial granulations, since which time the stools have remained negative on repeated examinations for typhoid bacilli

SUMMARY

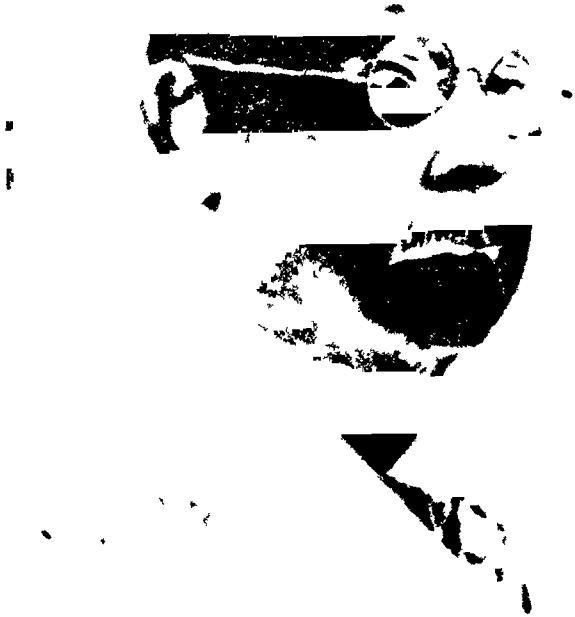
This case is shown because of the following rather unusual features First, repeatedly negative stools at the end of an attack of typhoid fever Second, repeatedly positive stools after the development of an acute cholecystitis during convalescence Third, pure culture of the *Bacillus typhosus* in a suppurative cholecystitis Fourth, persistence of positive stools after cholecystectomy, probably due to the common and right hepatic ducts containing stones which acted as a focus Fifth, repeated negative stools following removal of the common and right hepatic duct stones That these were acting as a focus is indicated by the recovery of *Bacillus typhosus* from the biliary tract for a short time after complete removal of the gallbladder

MEMOIRS

JOHN JENKINS BUCHANAN

1855-1937

JOHN JENKINS BUCHANAN, whose death occurred August 24, 1937, had one of the most brilliant surgical careers in the history of western Pennsylvania. His success as a surgeon and a teacher of surgery was to a great extent influenced by his background. He was descended from a line of



JOHN JENKINS BUCHANAN, M.D.

Scotch-Irish and Welsh forebears who distinguished themselves as theologians, educators and organizers. His two great-grandfathers served as Revolutionary soldiers, and another of his ancestors was responsible for founding Lafayette College in Pennsylvania, which he served as its President for 14

years, later serving as President of Washington University at Lexington, Virginia, until the Civil War. Doctor Buchanan's grandfather was a well-known clergyman, as was his uncle who distinguished himself as a leading educator of southeastern Ohio.

His father, Dr. James G. Buchanan (1825-1909), established his practice in Wellsville, Ohio, and was appointed Railroad Surgeon when the rails were first laid from Cleveland to Wellsville. For 50 years, until the time of his death, he served as Surgeon to the railroad lines which were incorporated into the great Pennsylvania Railroad System. This service was continuous with the exception of a four year interval when he served his country as Military Surgeon in the Union Army during the Civil War.

Doctor Buchanan was born at Wellsville, Ohio, in 1855, and received his primary education in the public schools there, and later in Allegheny City (now the North Side of Pittsburgh), where the family moved in 1866. He pursued a classical course in the Preparatory Department of the Western University of Pennsylvania (the present University of Pittsburgh), passing on to his collegiate course from which he graduated in 1877, and received his master's degree in 1880. His medical education was received in the University of Pennsylvania at Philadelphia, where he won his M.D. degree in 1881, with the first class required to take a three year course. After serving his internship at the Western Pennsylvania Hospital, he settled down to a general medical and surgical practice and received the appointment as one of the surgeons to the Pennsylvania Railroad Lines west of Pittsburgh. He soon began to operate on every surgical case he felt competent to undertake, many of these operations being performed in private houses, because the patients were generally poor and prejudiced against hospital treatment. He established a surgical clinic at the Pittsburgh Free Dispensary, where his first public surgical work was performed.

In these early years he served for a brief time on the staff of the Allegheny General Hospital, but, in 1891, when he was appointed Surgeon to the Mercy Hospital, his real life work began, for he served that institution faithfully and continuously from that time until his death. In 1921, he was appointed Chief Surgeon and Chief of the General Staff. Aside from his work at Mercy Hospital, he found time to organize the Surgical Departments of the Pittsburgh Hospital and Columbia Hospital, acting as Chief Surgeon of the former institution for nine years, and the latter for six years.

His teaching career began in 1901 with his appointment as Professor of Surgery and Clinical Surgery in the Western Pennsylvania Medical College now the Medical School of the University of Pittsburgh, and continued with a brief interval until 1936. It is impossible to estimate the influence of his teaching on the development of surgery in western Pennsylvania.

Doctor Buchanan's influence extended to the field of medical literature, to which he was a frequent contributor of papers on surgical subjects. In 1886, he collaborated in the publication of the Pittsburgh Medical Review, with the watchword "No secret proprietary nor Trade-Mark medicines advertised in

this journal " Rather than break this rule, the editors made up the deficits incurred in its publication from their own scanty earnings This journal later became the direct progenitor of the Pennsylvania Medical Journal, the present organ of the Medical Society of Pennsylvania The Library of the Pittsburgh Academy of Medicine was an outgrowth of the Pittsburgh Medical Library which Doctor Buchanan organized in 1891 He was actively interested also in the Library of the Mercy Hospital, and fostered its use among the Staff members

Doctor Buchanan was an indefatigable worker and a disciplinarian, maintaining his interest and supervision of the affairs of the hospital until he died His enthusiasm and unswerving loyalty to the ideals of the profession, his mastery of detail and his keen sense of humor combined to make him an ideal teacher and administrator He was a true friend whose counsel and advice were sought by his professional brethren, young and old His greatest relaxation was to pore over old books on special subjects in which he was interested, particularly very old medical works Although he had no hobby, his greatest pastime was motoring to new places

Doctor Buchanan was a charter member of the International Society of Surgery, and in 1911 was elected to Fellowship in the American Surgical Association He was a founder and life member of the American College of Surgeons serving on the Board of Governors continuously from 1916 until his death He was also a member of the Committee of Standards from Pennsylvania from 1916 through 1920, and of the Pennsylvania State Executive Committee which he served as Chairman In the late 80's and early 90's Doctor Buchanan was Recording Secretary of the Allegheny County Medical Society and in 1920 was its President

Besides his wife, Ellen Grier Buchanan, whom he married on June 30 1887 he leaves two sons to carry on the surgical and professional traditions of the family Dr E P Buchanan, a surgeon at Mercy Hospital, and John G Buchanan, a prominent Pittsburgh attorney

In January 1936 Doctor Buchanan's colleagues and members of various civic groups joined to pay tribute to him as one of Pittsburgh's most useful and public-spirited citizens At the testimonial dinner given in his honor, he spoke the words which best expressed his lifelong ambition which he fulfilled so well

"It will be the pride of my life if, when I pass, I shall leave a coterie of men whose natural abilities I have been able to shape in a surgical way I know of no higher compliment to any man than the approval and good will of the fellows of his craft"

OTTO C GAUB

ALLEN BUCKNER KANAVEL

1874-1938

QUIET, unassuming, friendly, with a genuine and alert interest in his profession and life and a kindly judicial temperament given but to a chosen few, Allen Buckner Kanavel's memory will continue to exert his influence upon



Photo by Du Bois

ALLEN BUCKNER KANAVEL, M D

surgical thought and procedures. The contribution he chose to leave to surgery above all else was the surgical training, the stimulus and interest in sur-

gical progress he was able to pass on to his younger associates. Thus, he felt, would live on after other more scientific contributions had passed.

The son of a Methodist minister, Doctor Kanavel was born September 2, 1874, in Sedgwick, Kansas. After graduating from the college of liberal arts at Northwestern University, he entered the medical school and was graduated with honors, in 1899. He spent six months in Vienna in postgraduate study, and then entered the Cook County Hospital for his internship. Immediately thereafter he became associated with the department of surgery at Northwestern University Medical School and remained a member of its surgical faculty to the time of his tragic death.

He was impressed early in his surgical career, with the uncertain and haphazard treatment given to patients with infections of the hand. After ten years of patient, meticulous study of the anatomy of the hand and the prosecution of a wholly original method of investigating the tendon sheaths and fascial spaces of the hand he published a monograph on the subject, in 1912. This work remains today as his most important contribution to surgical science and affords a basis for our present and future knowledge of the efficient care of this common and often seriously disabling condition. It is given but to a few to make such a fundamental addition to surgical knowledge.

However, he was introduced into a surgical practice before the day of surgical specialism and was keenly interested in abdominal, neurologic, thyroid and plastic surgery. In at least two of these fields he was a pioneer in Chicago and through his interest and help stimulated those who came in contact with him to carry on the torch he handed them.

From the inception of Surgery, Gynecology and Obstetrics, he was closely associated in its development and continued to direct its activities. Its contents speak far more eloquently than words of the time, effort and thought he gave to it as associate editor and editor. He strove to make it a vital force in aiding the practitioners of surgery in America, those men not associated with teaching centers, to keep abreast of the rapid changes constantly going on in surgical practice.

Apart from the respect and admiration his surgical ability and judgment commanded, he was loved for his constant adherence to the principles of his philosophy of life. He was quick to recognize and listen to the opinions of others regardless of their station or age. He was a great believer in the adage that time heals all difficulties and, therefore, avoided controversy, yet when dilatory tactics, brought about by differences of opinion, threatened a patient's welfare he was quick to act and assume full responsibility for his judgment. He had a simple, homely, charming manner, a shrewd common sense which transcended a more extensive complicated scientific theoretic knowledge, and an unfailing courtesy and kindness. He had a genuine interest in people, particularly the young men in medicine, and he was quick to recognize and to reward merit, without thought of his own personal fortunes or ambitions. With many interests outside his profession he was able to devote himself in his later years to their development. These interests in

geology, astronomy and books were a part of his plan of life formulated many years before his actual retirement from the practice of surgery, although he never lessened his interest in the advancement of surgical thought and teaching. Occupied throughout his life by an intensive study of obvious and practical surgical procedures, he strove to advance the frontiers of medical knowledge, to emphasize that an unselfish service to humanity, personal and professional honesty, the desire to seek new truths, industry, broad culture, judgment and imagination, even more than technical efficiency, are the qualities to be desired by every surgeon, worthy of the name.

With a mind filled with ideals, a soul possessed of kindness and a sympathetic understanding of all human frailties, he leaves behind him a well-spent life, an example for younger surgeons to emulate and to those of us who loved him, a memory to be revered.

LOYAL DAVIS

JOSEPH AUGUSTUS BLAKE

1864-1937

FROM the Dean of the College of Physicians and Surgeons, when Doctor Blake was Professor of Surgery, comes this letter

- -



JOSEPH AUGUSTUS BLAKE, M.D.

"Joseph Augustus Blake was born in 1864 in California where his father was serving as state geologist. Later, when the family moved to New Haven, he naturally, following in his father's footsteps, graduated from Yale College in 1885. He then spent a year in the laboratory of Russell H. Chittenden and, equally naturally, devoted most of his time as a medical student in the anatomical department of the College of Physicians and Surgeons, where he graduated as M.D. in 1888.

"His bent was distinctly scientific by inheritance, environment and education. He served as intern in St. Luke's Hospital and by 1890 was an attending surgeon in St. Luke's and Harlem Hospitals. He continued to develop the scientific features at the college, as a demonstrator under the leadership of the distinguished anatomist George S. Huntington, and always made an academic background to his surgical career. He was assistant to William T. Bull and later full attending surgeon at Roosevelt and Presbyterian Hospitals where he helped to advance the instruction of undergraduates into the surgical wards.

"Doctor Blake always took a broad and catholic view of medical education and hospital development. It was he who first suggested the present site as the best for the newly organized medical center combining the Presbyterian Hospital and Columbia's College of Physicians and Surgeons.

"Doctor Blake as a surgeon showed a complete development of the trained physician. His powers of diagnosis were exact and thorough, both in his methods of eliminating internal medical diseases and in differentiating an existing surgical condition. He always started his operations with a definite diagnosis and discarded the easygoing habit of many colleagues to make his surgical diagnosis with his knife. As a teacher he presented his material in a clear and complete form and left his students to catch up with him. He never approached his subject at their level but usually left it higher than they could reach without personal and individual study on their part."

SAMUEL W. LAMBERT

Doctor Brewster, closely associated with Doctor Blake in their professional and educational careers, writes as follows:

"As a wise and generous colleague, a helpful and intelligent co-worker, a gifted and resourceful surgeon, and, as an intimate and loyal friend, I have known Dr. Blake, esteemed and admired him for fifty years.

"By a singular coincidence, our professional lives exhibited an unusual parallelism. For nine years we served together as Assistant Demonstrators of Anatomy in the College of Physicians and Surgeons. Both were transferred on the same day to the Surgical Department, as Instructors in Clinical Surgery. Both passed through the various intermediary grades, eventually to become Professors of Surgery in the same institution.

"In hospital positions we also followed similar lines. After serving as Assistant Visiting Surgeons, he at St. Luke's, I at the City and at Mt. Sinai Hospitals, we both were appointed on the same day as Junior Surgeons.

to the Roosevelt Hospital he on the second division with Dr. Bull, I on the first with Dr. Wen. On the retirement of Dr. Bull and Dr. Wen, we both were advanced to the rank of Senior Surgeons. Also we both served, but at different periods, as Attending Surgeons at the Presbyterian Hospital.

"During the World War we both acted as voluntary surgeons in France, he as Attending Surgeon to the American Ambulance at the L'ecole Pasteur in Paris. I at Hospital B, at Juilly. S. et M. about 30 kilometers north of Paris.

"After the United States entered the War, we both were commissioned and served in the A.E.F. as operating surgeons in various military hospitals, and at a later period as Consultants. At the end of the War each of us retired with the rank of Colonel.

"Doctor Blake made many important contributions to surgical literature, covering his work in clinical surgery, research in the laboratory of experimental surgery, and in surgical pathology.

"As a diligent student and observer, a clever and mechanically-minded technician, he originated better methods of approach in deep seated lesions, new and ingenious methods of avoiding, lessening and treating surgical shock. He invented new instruments and devices to shorten and make safer operative procedures in gravely debilitated and handicapped patients.

"His wise and sane judgment, his unusual diagnostic skill, his transparent honesty and pleasing personality won for him many friends and brought to him many patients of all classes, as well as many professional colleagues who relied upon him for help in meeting their difficult and often obscure problems. These qualities and his outstanding early successes placed him in the foremost rank of American surgeons.

"I have always felt, as have many of his other friends and associates, a sincere regret that Dr. Blake did not publish in full an account of his long experience in military surgery.

"Entering the service of the American Ambulance in Paris, a few weeks after the beginning of hostilities, he served continuously and without interruption until the end of the War.

"His experience in the treatment of battle casualties was probably larger and more extensive than that of any other American surgeon. Realizing as he did the disastrous results which followed the plan adopted by the military authorities during the early months of the War, of transporting the great majority of the grave injuries to hospitals in the rear, often requiring several days without surgical treatment, or with the most inadequate procedures at the first-aid or temporary dressings stations, the grave infections such as those by the streptococcus, gas-producing organism, tetanus, *etc.*, as well as the extensive gangrene that followed delay, where important blood vessels were injured, or impeded circulation which resulted from tourniquets or constricting bandages, as well as the added trauma produced by untreated or badly splinted fractures of the extremities, led him to use all his influence to change these unfortunate conditions, to those in which such grave injuries could receive definite

and adequate surgical treatment before transportation to the hospitals at the rear, a plan which was later adopted by all the Allied Armies

"A record of the many and great advances which he made and advocated, especially in the treatment of such grave conditions as compound and gravely infected fractures of the extremities, the changed and more scientific methods he devised and employed in injuries of the abdominal, pleural, and cranial cavities, as well as the various changes which he made in splinting, extension, and postural apparatus, would all be of the greatest service to military surgeons in any future war

"Wholly apart from our professional relations, I always found Dr Blake a charming and delightful companion on vacational excursions. Our common love of the woods, mountain climbing, fishing and hunting, brought us together on many occasions, and I shall always cherish and remember with unalloyed pleasure our outings together in the Adirondacks and in the Canadian woods"

GEORGE E BREWER

Dr Walton Martin assisted Doctor Blake on his staff at Roosevelt Hospital as an Assistant Attending Surgeon. They were an extraordinarily gifted pair to work for. Writing "of him as I knew him in the days at Roosevelt Hospital," he states, 30 odd years later, that he was "the greatest surgeon I have ever come in contact with"

WALTON MARTIN

Dr William C. Clarke, after completing a surgical internship in the New York Hospital, where he worked with many of Doctor Blake's surgical seniors and contemporaries, taught histology at the College of Physicians and Surgeons. He soon came to see the importance of the microscopic study of the tissues in surgical diseases and gave his life to it. It is unnecessary to write of his contributions to Surgical Pathology, for he was its pioneer in the "P & S" under Doctor Blake. This inspiring teacher pays his tribute

"In an association of over forty years with the medical men of the College of Physicians and Surgeons and several hospitals associated with the College, from the last years of Stimson, Hartley, Bull, Wen and McBurney, to the present, Dr Joseph A. Blake stood out, preeminent. There were reasons. Truth was the basis for his evaluation of clinical evidence, not human emotions. He rarely was wrong in a diagnosis. His surgical judgment was referred to as superb. Gifted technically, with the ability to execute ably, his surgical results were of the best. At the same time raised in the highest ideals of his profession, he was 'a real doctor,' and his patients had deep respect for, and confidence in, his opinions, ability and judgment.

"Last summer he had built what proved to be his last shop for his wood working tools. 'Down East' in Maine he personally packed those much loved machines and tools and with equal care unpacked them in their new home in Litchfield. There were thirteen machines, and two thousand and five tools by actual count. Some of them he had devised himself and many he had actually made.

"I never remember his resorting to the so-called 'differential diagnosis method' as a procedure, in which the composite of many patients are invoked having no connection with the single patient before him. He was a reader of evidence in the patient before him. An unusual accuracy of vision of what happened in living man caused people to say it was intuitive and, indeed, he seemed unconsciously aware that a patient did, or did not, have appendicitis, or carcinoma or some other such disease. Once his mind was made up, he wandered little in probabilities—he acted.

'He was a lover of nature—a biologist, a physician, a surgeon, and always a true scientist.'

WILLIAM C. CLARK

Doctor Russell knew Doctor Blake as an assistant and associate in his surgical practice. He writes as follows:

"My association with Dr. Blake was, fortunately for me, a very happy and instructive one. He was my quiz master in anatomy, during which time I acted as his prosector.

"From 1901 to 1912 I was closely associated with him in Surgery. He combined to my way of thinking more things of the master surgeon than anyone it has been my lot to know. A great anatomist, a good pathologist and a real physicist—added to this he possessed a vast knowledge of surgery, and he had that great gift—Judgment—of what to do and when to do it. 'Corn Field sense' in rugged terms—an invaluable asset. He had an inspiration for planning new operations and applying them at the proper time. He was a great teacher—one of the greatest, in his way of imparting knowledge, one had to listen and absorb, for he never rammed his opinion down one's throat.

"I have always thought of him as one of the great surgeons of history. Last spring he made Surgical Rounds with me at the Roosevelt Hospital, on the Service he had headed with distinction for many years, and he was as keen and as interested as of old."

JAMES I. RUSSELL

Doctor Whipple, now holding the Professorship of Surgery, Doctor Blake held when he first knew him, was appointed to the Presbyterian Hospital and the P & S teaching staff by Doctor Blake, and knew his quality as an educator, surgeon, and a friend, as few ever did.

"Of the many outstanding qualities that characterized Doctor Blake as a surgeon's surgeon, the one that stood out constantly was his forthright honesty. He was always his own severest critic and would point out his errors in judgment and technique to us, his admiring apprentices, which we never would have noticed had he not called our attention to them. His influence over the younger group of surgeons working with him was permanent because we all knew he said what he meant and meant what he said. There is no doubt in my mind that his example in this respect played the greatest part in setting a standard of fairness and of rugged honesty in his department, in his hospital.

and in his surgical service which has stamped every surgeon who had the privilege of training under him and working with him. It was and is a mark of distinction to be known as a Blake man."

ALLEN O. WHIPPLE

Surgery, from 1904 to 1914, that I knew was intimately associated with Dr. Joseph A. Blake. So subtle are the essential traits that make a preeminent human character that they well might baffle description. To be asked to write of him brings difficulty with the honor.

By heritage and environment, he had an inquisitive, scientific interest in the truths of nature. Like an artist, he was intensely sensitive to impressions. As a genius, he used them to human advantage in a career that was once described as a "daily duel with death." He saw with his eyes and felt with his fingers what other men couldn't. He thought creations and saw essentials that other men didn't.

But there was more than that.

There was manual skill and a love for it. Head and hand went hand in hand and the work of his hands seemed eloquent. Those who watched, and the students he taught, thought so.

Simplicity dominated. Essentials were his aim. It was the point that mattered that counted with Blake. Seldom, in the nature of one man, have versatility and simplicity been so combined. Many a life lost in complexity was saved by this simplicity.

An "extraordinarily puzzling ward case" was once surrounded by an extraordinarily puzzled crowd of visiting surgeons from other parts of this country and Europe. An unusually capable intern had seemingly covered every possible detail of the patient's record in elaborate detail. It was painfully evident that the case remained a mystery to the great group of illustrious clinicians. Every sort of suggestion had been made. Finally, it was Blake's turn. He asked two simple questions. The patient said "yes" and then said "no." The mystery was solved and everyone knew the answer.

Surgery seemed so simple when he did it that it was almost dangerous for young students to watch him. It looked so easy. To the initiated, it was inspiring. Those who helped him kept many choice memories. May I tell you one?

Thirty years ago abdomino-perineal resections for rectal cancer were not done as frequently, nor successfully as today. Blake did almost 20 in a row with no deaths. But there were many hard battles. Some showed wisdom and courage ahead of his time—indeed noteworthy, any time. A difficult one was finished, after three hours' work, one Saturday. Pelvic floor closure was difficult and deep. Sunday noon there was vomiting and all was by no means well. It took courage, plus wisdom, to open the wound and lift a prolapsed loop of gut out of the pelvis—30 hours after so serious an initial procedure. But he did it and the man got well.

Few knew more than he of camping trips, fishing tackle, farm problems,

shotguns bird dogs, wild animals and natural phenomena of varied sort. Few shots of his went wild. He could bag most birds with least powder, noise and smoke. A nicety of skilled technique enabled him to mend motor cars, microscopes and men.

There was great kindness of heart toward patients. Deeply attached, grateful and loyal, they boasted of what he had done for them. Doctors besieged him, wealth wanted him, but a meticulous, personal attention to "ward dressings" was conspicuous. The sick poor were his devoted friends.

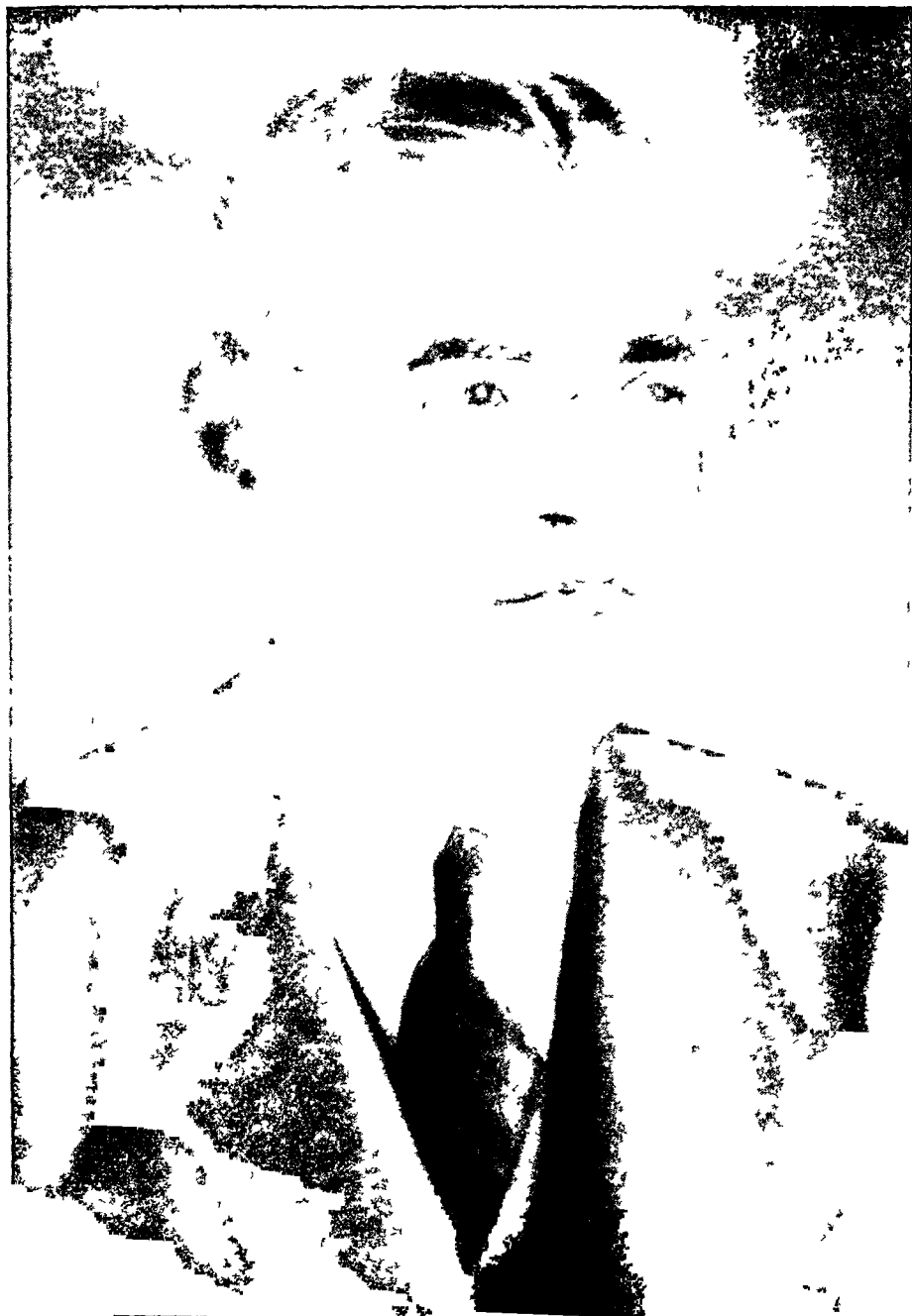
Whether peritonitis, herniae, anatomy of the brain, bowel surgery, lung, pleura and heart problems, war wounds or fractures will be most associated with Doctor Blake's name makes no difference. He gave the touch of Midas to them all.

HUGH AUCHINCLOSS

ROBERT BATTEY GREENOUGH

1871-1937

DR ROBERT B GREENOUGH, a member of the American Surgical Association since 1911, died suddenly from cardiac disease February 16, 1937, at the age of 66



ROBERT BATTEY GREENOUGH M D

Doctor Greenough was born in 1871 in Cambridge, Massachusetts. He entered Harvard College, graduating, cum laude, in 1893, and received the degree of M.D., cum laude, from the Medical School in 1896. He completed his medical education as house officer at the Massachusetts General Hospital and later studied in Vienna where he became particularly interested in tumor pathology, and although primarily a surgeon, this undoubtedly laid the foundation for his interest in cancer.

On his return to Boston he became the assistant to Dr. John Collins Warren, which position he held until his appointment to the Surgical Staff of the Massachusetts General Hospital. He served the Hospital in various positions until 1931 when he retired with the rank of Visiting Surgeon to become a member of the Consulting Staff.

During the World War he went to France with the First Harvard Unit as Surgeon and executive officers at the American Ambulance in 1915. After the entrance of the United States in the war he was appointed Lieutenant Commander and was in charge of the Surgical Service at the Naval Hospital in Chelsea.

He was actively connected with the Harvard Medical School, receiving the appointment of Assistant in Surgery in 1901 and Assistant Professor in 1910 which position he held until 1931.

His executive ability was recognized by all and he was called upon to fill many responsible positions. Among the positions held by him the following may be mentioned:

President, American College of Surgeons, 1934-1935

President, Massachusetts Medical Society, 1929-1931

President, Boston Surgical Society, 1928-1930

Secretary, American Surgical Association, 1922-1926

President, American Society for the Control of Cancer at the time of his death.

The study of tumors may be said to have been his life's work and his first contribution to literature, Plummer's Bodies in Cancer, was published in 1901.

When Doctor Greenough became associated with Doctor Warren, the latter was Co-Trustee with Doctor Oliver of the Caroline Brewer Croft Fund for Cancer Research. In 1909 this fund was combined with others and placed in the hands of the Cancer Commission of Harvard University. Doctor Greenough was appointed Secretary of the Commission. In 1912 he took an active part in the building and organization of the staff of the Collis P. Huntington Memorial Hospital for Cancer Research, and acted as Director of the Commission and Surgeon to the Hospital from 1915 to 1929. While recognizing the value of research work he saw no reason why members of the present generation who might be suffering from malignant disease should not have the advantage of the best known diagnostic facilities and treatment. The Consultation Cancer Clinics developed under him at the Huntington Memorial and Massachusetts General Hospitals have served as

models for those advocated by the American College of Surgeons and universally adopted throughout the country

Besides his professional ability as a surgeon and executive, he had the unusual faculty of making no enemies. If discussion arose in a committee or other meeting he would consider fairly the dissenter's point of view and bring the matter under discussion to an amicable settlement satisfactory to all concerned.

Outside of his profession he was a delightful companion and had a host of friends. It was the writer's privilege to have known him and his family intimately, and a trip on vacation taken with him was a delightful experience.

His death has been keenly felt by his medical colleagues and his many other friends.

CHANNING C. SIMMONS

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OBSERVATIONS ON THE MODE OF ACTION OF SULFANILAMIDE AND ITS APPLICATION TO SURGICAL INFECTIONS

JOHN S. LOCKWOOD, M.D.

PHILADELPHIA, PA.

FROM THE SURGICAL BACTERIOLOGY LABORATORY OF THE HARRISON DEPARTMENT OF SURGICAL RESEARCH, SCHOOLS
OF MEDICINE, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

THE DISCOVERY of the effectiveness of sulfanilamide in hemolytic *Streptococcus* infections has reopened the entire field of chemotherapy in bacterial diseases. It is now generally recognized that sulfanilamide therapy, properly conducted, will bring about a high percentage of cures in many types of invasive infection and septicemia which until this drug was introduced, had been almost uniformly fatal. The surprising results of sulfanilamide therapy have created new problems for those interested in fundamental aspects of the control of bacterial invasion. The lessons which may be learned through an intensive study of the mechanism of sulfanilamide action may find widespread application to other chemotherapeutic problems. Further progress in this field is dependent upon a clearer understanding of the mechanisms by which the drug influences bacteria, and a more comprehensive knowledge of its toxic side-effects.

Since this new type of therapy has provided the surgeon with such an efficient weapon in the prevention and control of certain rapidly invasive infections, it is proper that laboratories of surgical research concern themselves with the fundamental problems which this new therapy has opened. Experiments which we have conducted in the Department of Surgical Research at the University of Pennsylvania offer, we believe, an answer to some of the perplexing problems which now confront us, and, in addition, provide a rational basis for the use of the drug.

Experimental Observations—The fundamental observations of Marshall and of Colebrook, and their coworkers, are of the greatest importance to anyone interested in this field. Marshall¹ has demonstrated that sulfanilamide is quickly absorbed when administered either orally or parenterally, and becomes distributed with surprising uniformity throughout all the tissues and body fluids. It is rapidly excreted by the normal kidney, much of it in unaltered form. By repeated dosage of the drug, at short intervals, an equilibrium can be established in which the level of the drug in the blood and tissues remains fairly constant. These pharmacologic studies have supplied

the basis for the scheme of dosage now generally employed in practical therapy. The blood level of sulfanilamide must not drop below the therapeutically effective level until after the infection is controlled, or cured, if reactivation of infection is to be avoided. The optimum level for treatment of severe cases seems to be between 5 and 10 mg per 100 cc of blood.

Colebrook,² by finding that concentrations of sulfanilamide in blood of between 5 and 10 mg per cent provided the blood with a high capacity to kill *Streptococci* in vitro, made a significant contribution to the understanding of the mode of action of sulfanilamide. In his experiments it made no fundamental difference whether the sulfanilamide blood was obtained from a treated patient, or through the addition of the chemical to normal blood. Some time before the introduction of sulfanilamide, Hare³ had discovered that recovery from severe hemolytic *Streptococcus* infection was always accompanied by a marked increase in the bactericidal titer of the blood against the organism. Thus Colebrook's observation that sulfanilamide induced a streptococidal activity in blood could reasonably indicate that the absorption of the drug by the body tissues endowed them with resistance to *Streptococcus* infection similar in its effects to that occurring in the tissues of the patient convalescing from an active infection which had been overcome through natural immune processes.

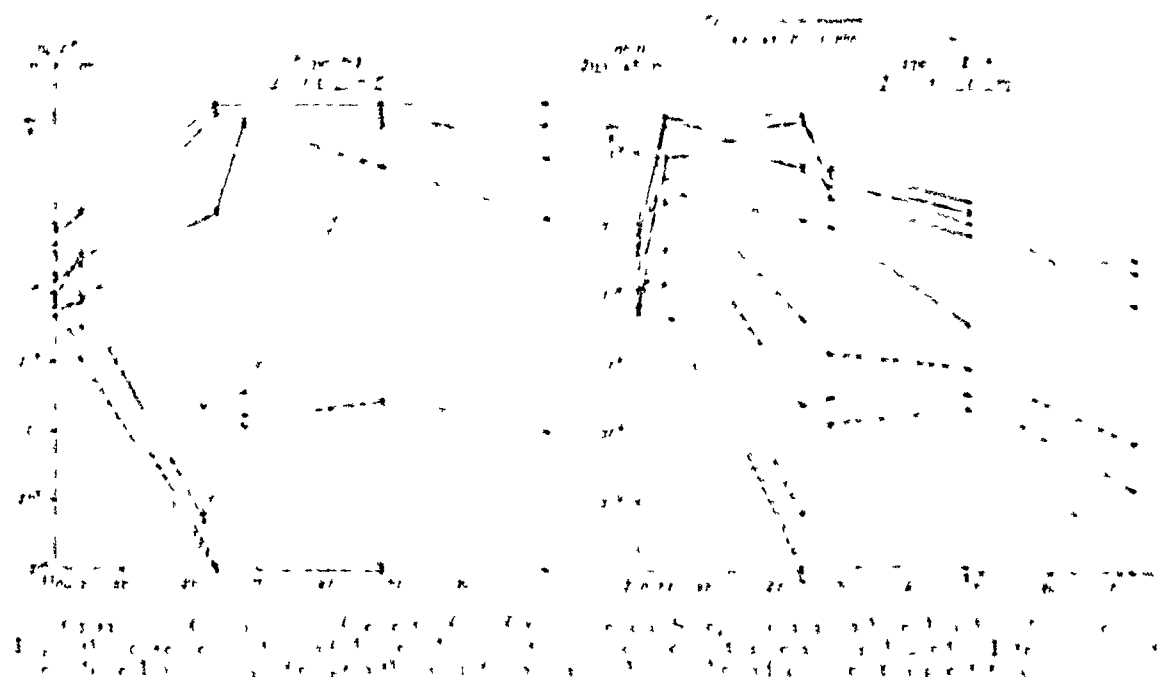
Our studies were prompted by the hope that an understanding of the mechanism by which blood containing sulfanilamide kills *Streptococci* in the test tube might provide a basis for explaining the action of the drug against organisms in the tissues and circulating blood.

Technic—We have made the effort to provide experimental conditions which would resemble tissue conditions during invasive infection as closely as possible. Hemolytic *Streptococci* of a virulent strain were grown for two hours in a medium containing 20 per cent of horse serum. This permitted testing the effect of the drug on young *Streptococci* in the encapsulated form, which Ward and Lyons⁴ have shown to be the most highly resistant to the destructive action of phagocytes. Moreover, it is quite possible that these young organisms, grown in serum-rich medium, resemble more closely than older organisms the rapidly multiplying *Streptococci* which are active in invasive tissue infection. The *Streptococci* were separated from the horse-serum-peptone culture medium by centrifugation and resuspended in human serum before adding them to the test blood. This was done in order to avoid the addition with the organisms of traces of the original culture medium. Blood was freshly obtained from the same normal human subject for each experiment and defibrinated with glass beads. Mixtures of whole blood, or its serum, and sulfanilamide, 10 mg per 100 cc, were prepared in small test tubes. For each tube containing sulfanilamide there was a corresponding control tube from which the drug was omitted, with all other experimental conditions identical. The *Streptococci* were then added in equal numbers to each of the tubes which were then sealed and rotated slowly on a mixing machine in the incubator at 37.5° C. At suitable intervals the tubes were

opened and, by making blood agar pour plates of 0.1 cc. of the contents, determinations were made of the number of living organisms in each mixture.

Chart 1 is a logarithmically plotted representation of the population curves, which demonstrates the effect of sulfanilamide under experimental conditions *in vivo*.

Growth of Streptococcus in Whole Blood—The increase in population of hemolytic *Streptococcus* in sulfanilamide-free whole blood proceeded rapidly from the start of inoculation so that in four hours there were about ten times as many organisms as at the beginning of the experiment. Similar studies at this time showed that active ingestion of many organisms by phagocytes had taken place, but phagocytosis under the conditions of the experiment was incapable of bringing about more than a transient reduction in the rate of multiplication. In 24 hours complete hemolysis of the blood had taken place and the bacterial population had increased to many millions. This level was



too high to permit direct counting of the colonies on the plates, even with the aid of the microscope.

When 10 mg. per 100 cc. of sulfanilamide was present a rapid trend toward sterilization developed which was clearly defined even at four hours. Therefore, the course of the population curve was related to the initial number of organisms implanted. The bloods containing the smallest starting population were sterile within 24 hours. The blood with the largest inoculation showed temporary reduction of the number of organisms, but sterilization did not occur. In fact, following the low point of population in this tube, which was at 24 hours, progressive outgrowth of organisms ensued. The blood became hemolyzed, and the final level of bacterial growth was identical with that in the sulfanilamide-free controls.

Discussion—In considering the significance of this experiment it is apparent that the possibility that phagocytosis is an active participant in the

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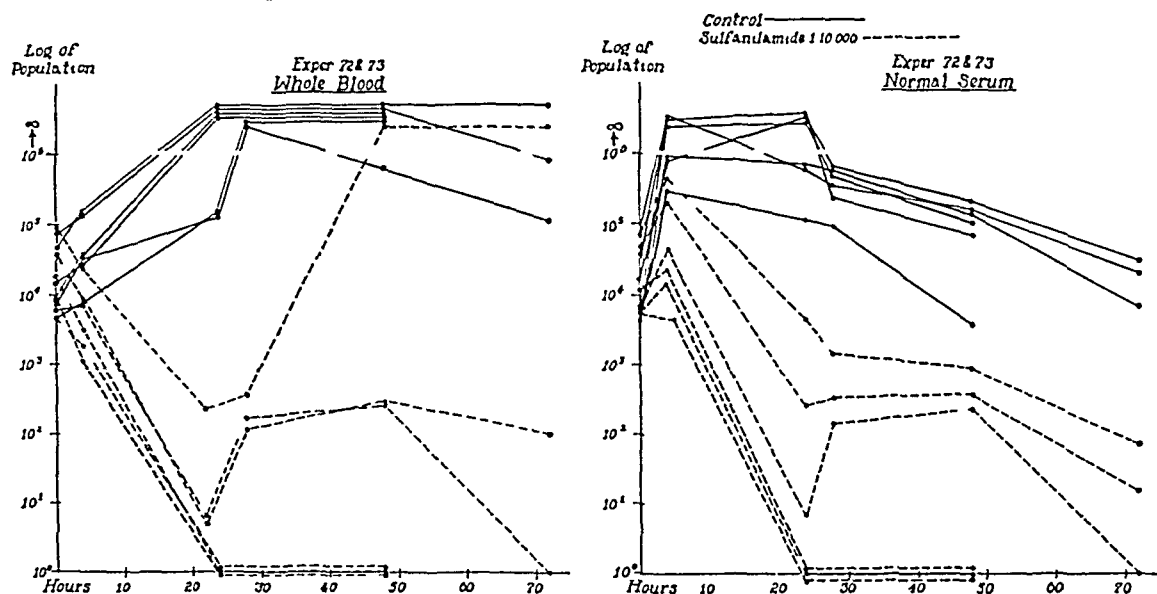


CHART 1—Comparison of effect of sulfanilamide on Streptococci in whole blood and in serum. Logarithmic representation of bacterial population in 0.1 cc at intervals indicated. Interruption of lines above Log 6.0 signifies growth to "infinity," i.e., the number of colonies too great to count.

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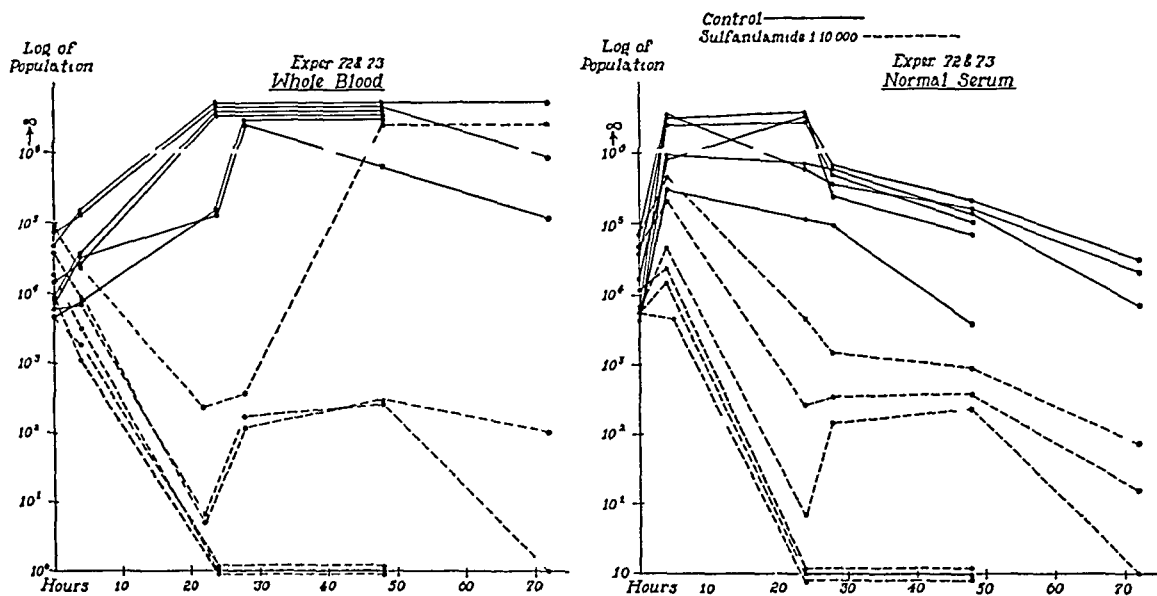


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Discussion—In considering the significance of this experiment it is apparent that the possibility that phagocytosis is an active participant in the

sterilizing action of sulfanilamide must be considered. The increased bactericidal action of the blood of convalescent patients has been generally believed to result from an increase in phagocytosis. One explanation of the bactericidal action of sulfanilamide in whole blood might be that the drug, by inducing a surface alteration in the organisms, increases their susceptibility to phagocytosis. One finds in the current literature that there is some indirect evidence which might tend to support the concept that sulfanilamide acts through promotion of phagocytosis. That this does not adequately explain the phenomenon is, however, evident when we find that normal serum, which contains no phagocytes, is just as effective a vehicle as whole blood for the action of sulfanilamide in destroying *Streptococci*.

Growth of Hemolytic Streptococci in Normal and Inactivated Serum—In comparing the action of sulfanilamide in whole blood, and in serum, the following points deserve mention.

(1) More rapid initial outgrowth took place in sulfanilamide-free serum than in sulfanilamide-free whole blood. This was due in all probability to the absence of any phagocytes in the serum.

(2) The sulfanilamide-free serum failed to support a level of bacterial growth as high as the sulfanilamide-free blood. This has been related in other experiments to the lack of products of hemolysis in the serum. In whole blood, the breakdown of blood cells produced by streptococcal hemolysin enriches the medium to such a degree as to permit greater numbers of *Streptococci* to continue multiplying.

(3) Sulfanilamide in the serum allowed a temporary, but slight, increase in population during the first four hours. Following this initial phase of limited outgrowth, there was a progressive trend toward sterilization, similar to that which developed in the whole blood containing sulfanilamide.

Discussion—The capacity of sulfanilamide to interfere with the multiplication and survival of hemolytic *Streptococci* in cell-free serum tends to rule out the mechanism of phagocytosis as a major essential participant in the action of the drug.

Normal serum, even without sulfanilamide, is not a suitable culture medium for *prolonged* survival of hemolytic *Streptococci*. This is shown in the controls by progressive reduction in the number of surviving organisms after 24 hours. The parallelism between curves obtained from the three sulfanilamide-containing tubes in which early sterilization did not take place, and the curves of the corresponding sulfanilamide-free controls, suggests that the effect of sulfanilamide might have been to exaggerate the inhibiting influence on streptococcal growth which is an attribute of normal serum. However, serum may be rendered much more suitable for prolonged multiplication and survival of *Streptococci* by the addition of small amounts of peptone. The major source of nitrogen in pure serum is the serum protein. The addition of peptone provides the bacteria with an additional, and more easily assimilable, source of nitrogen.

Bambridge⁵ has shown that some species of bacteria are unable to break

SULFANILAMIDE

down protein molecules to obtain essential nitrogen, and literally "starve to death" in a medium of serum protein or egg albumin unless predigested protein, in the form of peptone, is supplied to them. Apparently the virulent hemolytic *Streptococcus* can utilize protein to some extent, as evidenced by the rapid initial growth in population of the organisms in normal serum. Supplementary experiments have shown us that nonvirulent *Streptococci* almost completely lack the ability to grow in peptone-free serum. Data which we obtained suggested the possibility that sulfanilamide may produce its restricting action on the growth of virulent *Streptococci* in serum by interfering with their utilization of serum protein. The following experiment offers indirect evidence on this important point.

Influence of Peptone on the Action of Sulfanilamide—The population curves for hemolytic *Streptococci* in serum containing sulfanilamide were

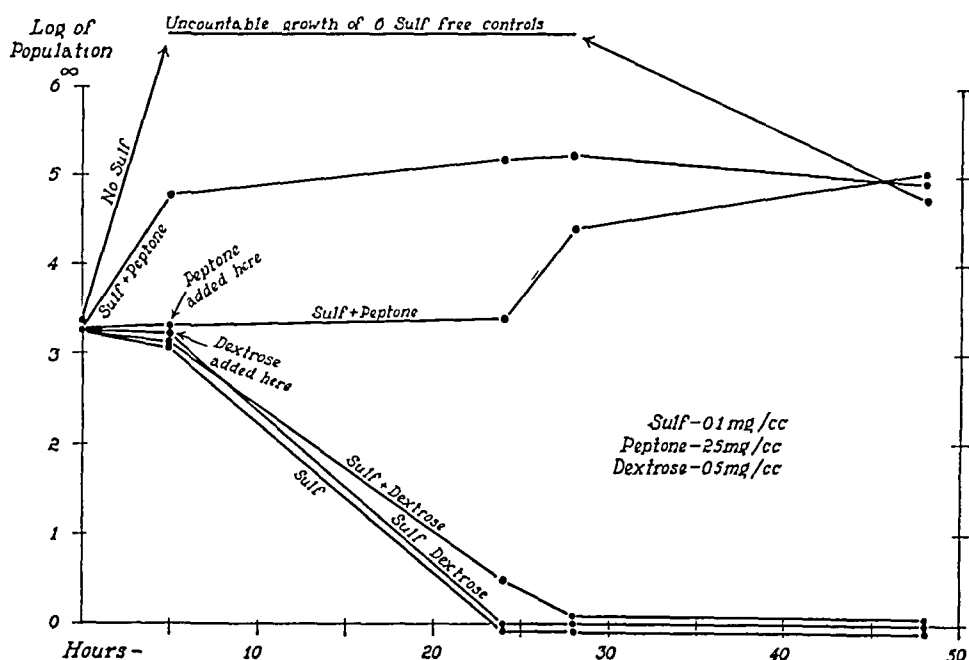


CHART 2—The effect of peptone on the action of sulfanilamide. The uppermost curve is the average of the six sulfanilamide free controls the populations of which were at uncountable levels for most of the period of incubation.

calculated as in the preceding experiments. In addition, the growth curves were estimated for serum-sulfanilamide mixtures to which a small amount of peptone had been added. In one instance the peptone was added at the beginning of incubation, and in another it was introduced after five hours of incubation. As a further control, there was added to other tubes of serum a small amount of dextrose, which, like peptone, may under some conditions stimulate bacterial growth. Chart 2 shows the effects of these substances on the population curves.

(1) No population increase occurred during the first five hours in serum-sulfanilamide tubes which did not contain peptone. A marked increase in population took place when peptone was present. The addition of dextrose did not encourage growth.

(2) The addition of peptone after five hours of incubation of the culture permitted survival of the *Streptococci* and eventual increase of population.

to the level of sulfanilamide-free controls. Failure to add peptone permitted the restricting effect of sulfanilamide to continue, and no living organisms remained after 24 hours.

Discussion—In many experiments of a similar character, employing different types of peptone, the inhibiting effect of peptone on the action of sulfanilamide has been constantly apparent. We believe that this evidence justifies the tentative conclusion that sulfanilamide interferes with the ability of virulent hemolytic *Streptococci* to use serum or tissue protein as a "food" from which to obtain nitrogen. If no source of nitrogen other than protein is present in the bacterial environment, the organisms cannot continue to multiply and the population dies out.

We hope that through study of the enzyme actions by which invasive

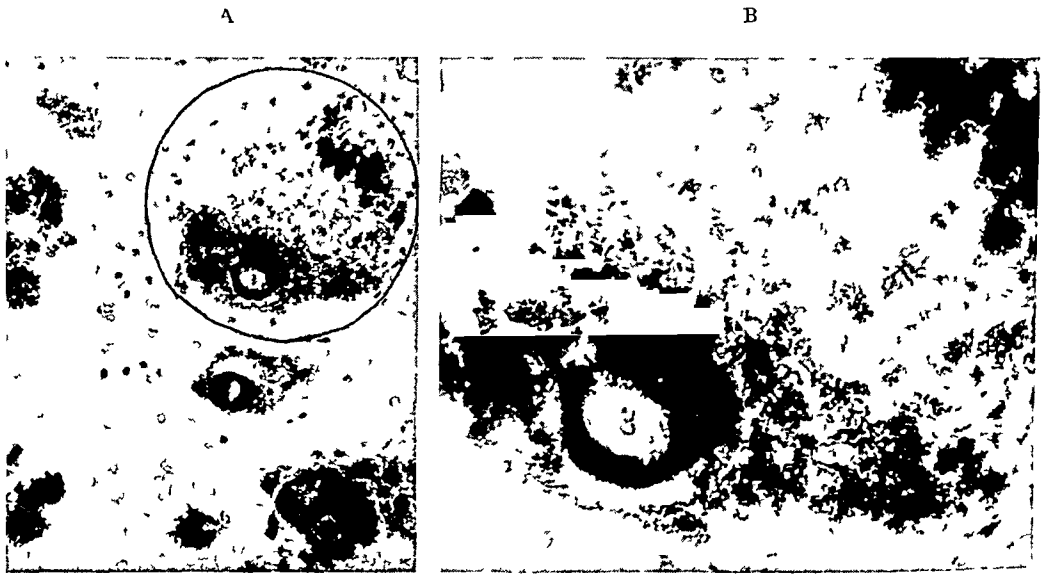


FIG. 1—(A) Illustrates a highly invasive infection and shows a photomicrograph of a section of the brain of rat dying 30 hours after introduction of hemolytic *Streptococci* into subarachnoid space through a cranial trephine. Note the grouping of masses of cocci around small vessels, complete absence of cellular exudate and organisms spreading through tissues which are architecturally almost normal ($\times 400$). (B) Higher magnification of (A) (circle). Note the cocci within a blood vessel, and absence of phagocytes ($\times 1,400$).

organisms attack protein we may obtain direct evidence which will prove, or disprove, the validity of this concept. It has been of interest to us to note, however, that this explanation of the action of sulfanilamide conforms with the clinicopathologic alteration induced by sulfanilamide in infectious lesions in patients and animals.

The course of *Streptococcus* infection in over 200 patients treated with sulfanilamide last year at the Presbyterian Hospital in New York City was studied by Dr. Alvin Coburn and myself.⁶ From this study it was concluded that the most striking effect of sulfanilamide was the suppression of tissue invasion in actively or potentially invasive infections. The patients with erysipelas, fulminating cellulitis, primary hemolytic *Streptococcus* peritonitis and meningitis were brought under control more rapidly and completely by sulfanilamide than the patients with the less virulent, more subacute

types of infections. The highly invasive *Streptococcus* lesions are characterized histologically by minimal changes in the tissue architecture at the peripheral zone of bacterial invasion. The organisms are actively multiplying in, and spreading through, tissues not yet digested by the action of inflammatory exudates⁷ (Fig 1A, B). In this type of process the organisms are apparently utilizing the proteins of the intact tissues for synthesis of their bacterial proteins, and in this type of lesion sulfanilamide acts with greatest effectiveness. Such a lesion may be compared to the infected normal serum of our experiments, the medium in which sulfanilamide has been shown to exercise a sterilizing action on *Streptococci*.

Furthermore, it appeared in our clinical study that the presence of necrotic tissue or pus in a lesion prevented sulfanilamide from acting upon the organisms with the same maximum effect which characterized its action on diffuse nonsuppurative infections. If an infection was treated after two or three days of progression, and some degree of localization or abscess formation had occurred, sulfanilamide seemed clinically to accomplish little more than to protect uninvolved tissues. Necrotizing tissue and pus contain peptone-like products of protein disintegration. It may be that the presence of this material in tissue lesions protects *Streptococci* from the full action of sulfanilamide through a mechanism similar to that which we have observed under experimental conditions. In the suppurative infections the bacterial environment is rich in peptones, the organisms are not dependent upon utilizing protein for survival, and are therefore able to resist the action of the drug.

CONCLUSIONS

- (1) The sterilizing action of sulfanilamide under experimental conditions is not dependent upon the participation of phagocytic cells.
- (2) Sulfanilamide in serum is capable of preventing the multiplication of hemolytic *Streptococci*.
- (3) The sterilizing effect of sulfanilamide upon hemolytic *Streptococci* in serum is prevented by the addition of small amounts of peptone.
- (4) Indirect evidence is offered to suggest that sulfanilamide acts upon hemolytic *Streptococci* by interference with their protein-digesting mechanism.
- (5) Some of the clinical results of sulfanilamide therapy are explained through these concepts of the action of the drug.

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TOXIC MANIFESTATION OF SULFANILAMIDE*

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It is obvious that for the proper use of any therapeutic compound a knowledge of its possible harmful effects is necessary. This is especially true in regard to therapy with sulfanilamide because this chemotherapeutic agent, while possessing a low degree of acute toxicity for both man and animals,^{1 2 3} is capable of producing a wide variety of undesirable side-effects in human beings.

We wish to discuss the toxic manifestations which have occurred during the course of sulfanilamide therapy in 335 patients at the Johns Hopkins Hospital, together with certain observations upon the recognition and control of such manifestations.

In our original report,¹ we noted the occurrence of certain cerebral toxic effects in mice and in human beings. These are among the most common toxic effects and consist of dizziness, headache, a loss of the ability to concentrate, a loss of normal reaction time, anorexia, nausea and, in some instances, vomiting. These manifestations by themselves have rarely been severe enough to warrant discontinuing the drug in ward patients but symptoms in this group are frequently very annoying to the ambulatory patient and may be severe enough to necessitate stopping the drug. It is of interest to note that sulfanilamide and alcohol tend to complement each other in their toxic effects, and because of this the use of alcohol should be discouraged in patients receiving sulfanilamide. The decreased mental acuity and dizziness which sometimes occur in the course of sulfanilamide therapy may render the ambulatory patient dangerous insofar as driving a motor vehicle is concerned. Professional motor vehicle drivers should be warned in this respect. Because of the frequency of these cerebral effects we feel that whenever it is practical the patient who is receiving sulfanilamide should be kept in bed—at least during the first days of treatment.

Cyanosis of varying degrees is almost a constant finding in patients treated with sulfanilamide. The mechanism of the production of the cyanosis is still in dispute. Marshall⁴ does not believe that the formation of methemoglobin is always responsible for the cyanosis while Wendell⁵ has stated that varying degrees of methemoglobinemia have been found in 200 patients treated with sulfanilamide. Despite certain dissident foreign observations,^{6 7 8} the cyanosis does not seem to be due to sulphemoglobinemia. We have noted intense cyanosis appearing within four hours after the ingestion of 15 Gm. of sulfanilamide, and on the contrary we have noted patients in

* These investigations have been supported by a grant from the Chemical Foundation, Inc.

whom large doses (3.6 to 7.2 Gm per diem) of sulfanilamide produced but mild degrees of cyanosis. We do not believe that the development of cyanosis, by itself, constitutes a dangerous toxic manifestation in the course of sulfanilamide therapy, nor do we believe that cyanosis is a contraindication to further treatment.

Clinical acidosis, as evidenced by the combination of hypernoia and a lowered CO_2 combining power, has been noted in 3 per cent of the 335 patients who comprise this study. As we have previously stated,⁹ the acidosis is accompanied by loss of sodium and potassium in the urine. Since we have adopted the routine procedure of prescribing bicarbonate of soda with each dose of sulfanilamide, we have not noted this toxic manifestation. The amount of bicarbonate of soda needed to eliminate the possibility of acidosis is from one-third to one-half of the dose of sulfanilamide. If sulfanilamide is being given by the parenteral route, the use of one-sixth molar* sodium lactate solution as the solvent for the drug will prevent the occurrence of acidosis. If acidosis should occur, then the oral administration of sodium bicarbonate or the parenteral use of one-sixth molar* sodium lactate solution is indicated.

Jaundice (without anemia) accompanied by a marked decrease in liver function has occurred but once in this series of patients. The jaundice rapidly disappeared and the liver function returned to normal soon after sulfanilamide therapy was discontinued. We do not believe that the previous existence of liver damage or jaundice is necessarily a contraindication to sulfanilamide therapy. This is especially true if the existing liver damage is the result of an infection in which therapy with sulfanilamide is indicated.

We have not noted any evidence of renal damage or irritation which could be remotely attributed to sulfanilamide. It is to be remembered in this connection that the damaged kidney does not excrete sulfanilamide easily, and care should be taken that sulfanilamide does not accumulate in the blood stream in patients with impaired renal function.

Dermatitis has been relatively uncommon in this series of patients with but 1 per cent of the group showing this type of toxic reaction. This figure is lower than that observed by Hageman and Blake,¹⁰ and by Schwentker.¹¹ In our experience the rash has always been similar to that of measles. All have been accompanied by some degree of temperature and all have cleared rapidly when the drug was discontinued. This procedure will do away with the possibility of a severe dermatitis of the exfoliative type developing. In one instance in which sulfanilamide was given again after the rash had disappeared, a mild dermatitis developed rather promptly. In but one case has the dermatitis seemed to be associated with a photosensitivity of the skin.

Simple fever has been the most common toxic reaction (6 per cent) noted in this series of patients. Frequently the question is asked as to how one differentiates the fever due to sulfanilamide from that due to the infection. It is interesting to note in this respect that in but one instance has this ques-

*.N.b., molar solution represents one containing 18.67 Gm per liter

tion had to be decided in the 22 patients in our series who developed fever as a toxic manifestation of sulfanilamide therapy. All of the other patients had had one or more days of normal temperature before they developed the drug fever.

The time of the occurrence of the fever is of interest. Two patients developed fever on the first day of therapy with sulfanilamide, four on the third day, one on the fourth day, two on the fifth day, two on the sixth day, four on the seventh day, two on the eighth day and five on from the ninth to the fourteenth day of treatment. Thus it is evident that fever may occur at any period in the course of sulfanilamide therapy.

In addition to simple fever due to sulfanilamide, we have noted that in almost all instances the patients developing a dermatitis, an acidosis, an acute hemolytic anemia or an agranulocytosis also show an early febrile response. Because of this, we have come to the conclusion that the appearance of fever constitutes an important warning sign in the control of patients being treated with sulfanilamide, and that sulfanilamide should be promptly discontinued in patients who develop an unexplained fever.

Inasmuch as simple fever is a fairly common toxic manifestation in the course of sulfanilamide therapy, the question of whether it is dangerous to resume treatment with the drug after the fever has disappeared is of importance. Our observations lead us to believe that it is impossible to predict whether a given patient will develop another febrile reaction if sulfanilamide therapy is resumed. However, because of the intensity and sharpness of the febrile reactions which have followed the restoration of sulfanilamide therapy in certain patients, we believe that it is wise to administer a test dose of 0.3 Gm. of the drug to patients who have previously had a febrile response to sulfanilamide. Then, if no febrile reaction occurs within 12 hours, it has seemed safe to continue with the drug. If, on the other hand, a sharp febrile response is noted, it is unwise to attempt further sulfanilamide therapy.

Anemias of the hemolytic type have occurred quite commonly in this series of patients. Fortunately, most of the anemias were mild in type and slow in developing. A drop in hemoglobin of from 10 to 20 per cent is a common finding in the course of sulfanilamide therapy, especially if the treatment is prolonged over a period of ten days or more. These slowly developing anemias are not accompanied by bilirubinemia, although increases in the reticulocyte count above normal limits are the rule after the hemoglobin begins to drop. Urobilin is almost constantly present. Our observations lead us to believe that these slowly developing mild anemias are not a contraindication to the continuation of sulfanilamide therapy.

Acute hemolytic anemias,^{13, 14} characterized by a rapid fall in the red blood cell count and the hemoglobin, a moderate to a marked leukocytosis, marked reticulocytosis, bilirubinemia, urobilinuria and in certain instances porphyrinuria, have occurred in 3 per cent of the patients included in this series. This type of toxic manifestation is one of the most serious encountered in the course of sulfanilamide therapy. These anemias have generally been severe enough

to necessitate one or more transfusions. They occur within 24 to 72 hours after treatment has begun. The maximal anemia generally develops within three days after the hemolytic process is initiated. All of these patients show a definite rise in temperature during the anemia phase. This toxic manifestation is more common in children than in adults. In one instance in which therapy with sulfanilamide was resumed the hemolytic process recurred.

The mechanism of this type of anemia is not as yet clearly understood but it would seem to be the result of an individual idiosyncrasy toward sulfanilamide. There is no evidence that any one type of infection predisposes an individual toward this form of anemia. Experience has shown that sulfanilamide should be discontinued if an acute hemolytic anemia develops.

Agranulocytosis has been reported in the course of sulfanilamide therapy^{15 16}. We have noted one patient, suffering from a gonococcal arthritis and urethritis, who developed this toxic manifestation toward the end of the third week of treatment. This patient showed the typical picture of agranulocytic angina. Treatment designed to rid the patient of sulfanilamide was immediately instituted, and within ten days he had made a complete recovery from this blood dyscrasia. The mechanism of the production of serious leukopenias and agranulocytosis by sulfanilamide is as yet unknown.

Sulfanilamide is excreted by the kidneys, as has been shown by Marshall¹⁷ *et al*. Therefore, when any type of toxic manifestations due to this drug occurs and it is desired to rid the organism of sulfanilamide as quickly as possible, large quantities of fluid should be given. The ensuing water diuresis will result in the rapid elimination of sulfanilamide from the blood and tissues.

CONCLUSIONS

Sulfanilamide produces many and varied toxic effects in human beings. However, we believe that if therapy with sulfanilamide is controlled by careful clinical and laboratory observations, the toxic manifestations of the drug will be recognized in their inception and no great harm will come to the patient. Detailed observations of the patient, careful temperature recordings and daily blood studies are exceedingly important in the care of the individual who is being treated with sulfanilamide.

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THE EFFECT OF SULFANILAMIDE UPON HUMAN, VIRULENT HEMOLYTIC STREPTOCOCCI

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IT IS a matter of easy confirmation that the addition of sulfanilamide to nutrient broth or human serum slows down the rate of multiplication but does not lead to the death of B-hemolytic Streptococci implanted in such media^{1 4}. This bacteriostatic influence cannot be said to constitute the sole mode of action of the drug because it is established that sulfanilamide enhances the bactericidal powers of human blood² in infected patients. The only known method whereby the body can destroy gram-positive Cocci is the process of phagocytosis and intracellular digestion. The effective action of sulfanilamide has been shown to depend upon the presence of phagocytic cells,¹ and it is reasonable to postulate that sulfanilamide has some action which renders this phagocytic mechanism more effective in killing hemolytic Streptococci. It is obvious, as observed by Reimann,³ that this streptococcidal effect must be attributable to one or more of three possibilities: (1) A specific activation of the reticulo-endothelial system, (2) an inhibition of toxin formation, and (3) an alteration in the capsule of the Streptococcus. It is instructive to discuss the findings of other workers in relation to these possibilities.

(1) *Specific Activation of the Reticulo-Endothelial System*—The reticulo-endothelial system may be considered to include the phagocytic cells and the specific antibodies of the serum. Sulfanilamide therapy does not alter the cytologic response to infection in experimental animals^{4 5}. There are no reported experiments which deal directly with antibody formation in sulfanilamide treated animals, but it is possible to evaluate this effect by a consideration of reported protection experiments. Mice survive the intraperitoneal injection of many lethal doses of Streptococci as long as sulfanilamide therapy is continued, but when the drug is withdrawn many of the animals subsequently die of their infection,⁶ and it is, therefore, unlikely that sulfanilamide therapy has stimulated an active immunity during the time of treatment. Seastone⁷ has demonstrated that the surviving guinea-pigs of sulfanilamide treated Group C-hemolytic Streptococcus infections are susceptible to reinfection. There is no evidence that antibody formation is specifically stimulated by sulfanilamide, and it may be concluded that the drug does not specifically activate the reticulo-endothelial system insofar as antibody production by that system is concerned.

(2) *Inhibition of Toxin Formation*—Bliss and Long¹ have remarked

that toxin formation is probably suppressed by virtue of the bacteriostatic action of sulfanilamide to a point at which the Streptococci "no longer produce enough 'leukocidin' and other toxic products to inhibit rapid phagocytosis" Osgood and Brownlee⁸ have observed that Streptococci grown in the presence of sulfanilamide produce less than normal quantities of hemolysin. From this it is argued that sulfanilamide inhibits the total toxigenic activity of Streptococci and thereby converts the organisms to "harmless saprophytes." The experimental evidence available at the present time does not appear to us to be sufficient to conclude that such an inhibition of toxin formation could be the adjuvant factor supplied by sulfanilamide in the bactericidal mechanism observed in the clinical use of the drug.

(3) *Alteration of the Capsule*—Levaditi and Vaisman¹¹ advanced the hypothesis that the action of the drug might be attributable to an inhibition of encapsulation. This viewpoint was not tenable after the demonstration of encapsulated organisms in the peritoneal cavities of treated mice,¹² but distinct degenerative changes have been observed in the morphologic appearance of Streptococci grown in sulfanilamide serum.⁴ Bliss and Long¹ have shown that the Streptococci in the peritoneal cavities of infected mice are more readily phagocytized in sulfanilamide treated animals than in normal controls. This increased phagocytosis in the absence of specific antibacterial antibody is evidence of an alteration in the surface or capsular antigen.^{9, 10} The truth of this is not denied by the histologic demonstration of a capsule because it is immunologically possible to differentiate between two types of morphologically identical capsules.^{9, 10} Hemolytic Streptococci in the human virulent phase are encapsulated and resistant to phagocytosis, whereas variants of attenuated virulence may be encapsulated and susceptible to phagocytosis. The failure of active immunization to occur in sulfanilamide treated animals is consistent with an antigenic alteration in the structure of the bacteria.

In the present report we wish to present the experimental data which demonstrate that there is a physicochemical alteration of the structure of B-hemolytic Streptococci grown in the presence of sulfanilamide. It was elected to perform these studies in human blood because there are many discrepancies between the infections in humans and those in mice. The F variant of the hemolytic Streptococcus is virulent for man but has little or no primary virulence for mice.^{9, 10} Sulfanilamide therapy does not protect mice infected with freshly isolated human strains or strains of low mouse virulence.^{5, 6, 12} The drug appears to have little or no effect on the established mouse infection,^{5, 6, 13, 14} whereas, it is only applicable to humans with pre-existent infections. The bactericidal effect of sulfanilamide is demonstrable in human blood but not in the blood of lower animals,^{2, 12} but this is probably due to the lesser phagocytic efficiency of the circulating leukocytes of these animals.

EXPERIMENTAL METHODS—(1) *Source of B-Hemolytic Streptococci*—The bacteria were obtained from blood cultures and direct platings of pus from human lesions. The strains were studied at the time of isolation to determine

whether one or more variants were present. Stock cultures were grown overnight in a meat tube, covered with mineral oil and stored in the refrigerator.

(2) *Cultivation*—The composition of differential blood agar plates and serum neopeptone water has been reported^{9, 10}. Sulfanilamide (Merck) has been added as dried powder to a concentration of 10 mg per cent prior to autoclaving, and desired dilutions in neopeptone water prepared.

(3) *Spontaneous Agglutination*—This technic has been reported⁹. Equal quantities of overnight culture and saline are placed in the water bath at 55° C for three hours, and read with the naked eye for agglutination.

(4) *Phagocytosis*—The complete details of this technic have been reported⁹. The resistance to phagocytosis of virulent variants was checked in every experiment by the use of infant blood or washed adult cells resuspended in a 1:8 dilution of homologous serum in saline^{9, 10}. Sulfanilamide blood was obtained directly from patients receiving the drug or was prepared by adding sulfanilamide (Merck) to freshly drawn, defibrinated blood.

(5) *Bactericidal Technic*—These tests were performed by the modified Todd technic¹⁶. Sixteen-hour cultures were serially diluted in homologous media without horse serum and added to tubes of the defibrinated blood. The tubes were sealed, rotated for 48 hours at 37° C and then cultured upright for 24 hours at 37° C. The contents of each tube were then washed into 5 cc of 5 per cent horse serum neopeptone water and incubated at 37° C overnight. Smears and cultures were made of these last named cultures to determine which of the bactericidal tubes contained bacteria.

(6) *Sulfanilamide Determinations*—The sulfanilamide levels of the blood and media were determined by the method of Marshall¹⁷.

(7) *P_H Determinations*—These observations were performed with the colorimetric method and checked by the electrometric technic.

EXPERIMENTAL RESULTS—(1) *Variation in Form of Colonies*—Gay and Clark⁴ observed that Streptococci grown in human serum containing sulfanilamide and then transplanted onto differential media gave rise to a mixture of virulent and avirulent colony forms on primary subculture which reverted to all virulent colony forms on subsequent subculture. This observation was confirmed and it was further found that normally grown Streptococci transplanted onto differential media containing 10 mg per cent of sulfanilamide also yielded a mixture of virulent and avirulent colony forms. Sulfanilamide-grown Streptococci transplanted onto sulfanilamide media produced all avirulent colony forms but subcultivation back onto normal media resulted in a reversion to the virulent colony form.

(2) *Spontaneous Agglutination*—The capsules of the virulent M and the attenuated M variants are morphologically identical, but the virulent variants are resistant to phagocytosis in the absence of specific antibacterial antibody and do not agglutinate spontaneously, whereas the attenuated variants are readily phagocytized and are spontaneously agglutinable^{9, 10}.

Table I shows the results obtained from an experiment in which virulent strains are rendered spontaneously agglutinable by progressive subcultivation.

in sulfanilamide media. Similar experiments, with many strains, have shown a great variation in strain susceptibility to this sulfanilamide-induced spontaneous agglutination, but practically all strains show some agglutination after three subcultures in 10 mg per cent sulfanilamide media. This agglutinability is attributable to an alteration in the structure of the organisms, because Streptococci which have been washed and resuspended in saline after growth in sulfanilamide media are similarly agglutinable and no alteration in p_H has been observed in the media used for these tests. The capacity for spontaneous agglutination is lost in the first normal subculture away from sulfanilamide media. It is concluded that continued growth in sulfanilamide media conditions a physicochemical alteration in the surface antigen of B-hemolytic Streptococci. It has been impossible to determine whether this change is due to an absorption of some substance onto the Cocci or to a direct modification of the capsule.

TABLE I

THE SPONTANEOUS AGGLUTINATION OF STRAINS PASSAGED IN SULFANILAMIDE MEDIA

Amount of Sulfanilamide in Media	Subculture					
	Strain "Gal "			Strain "Ber "		
	1st	2nd	3rd	1st	2nd	3rd
0 mg %	0	0	0	0	0	0
2.5 mg %	0	=	++	0	0	++++
5 mg %	0	0	++	0	++	++++
10 mg %	0	=	++	0	++	++++

TABLE II

THE PHAGOCYTOSIS IN AN INFANT'S BLOOD OF STRAIN "MCL"
PASSAGED IN SULFANILAMIDE

History of Culture Tested	Normal Blood	Sulf † Blood
33x in normal serum neopeptone	0 — 0%*	0 — 0%
32x in normal serum neopeptone, then 1x in sulf † serum neopeptone	0 — 0%	0 — 0%
3x in sulf serum neopeptone	90 — 18%	64 — 16%
33x in sulf serum neopeptone	121 — 36%	160 — 34%
32x in sulf serum neopeptone, then 1x in normal serum neopeptone	0 — 0%	0 — 0%

* 0 — 0% = 0 Streptococci phagocytized by 0 per cent of 50 cells counted

† Concentration of sulfanilamide used in blood and media = 10 mg per cent

(3) *Phagocytosis*—Table II shows the results obtained from a phagocytic experiment with infant's blood containing no demonstrable antibacterial antibody to Streptococci. It is shown that progressive subcultivation in sulfanilamide media renders the organisms susceptible to phagocytosis even in the absence of specific antibody, and that the bacteria revert to the phagocyte resistant form when they are subcultured into normal media.

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TABLE III

THE EFFECT OF ANTIBACTERIAL ANTIBODY AND PASSAGE IN SULFANILAMIDE UPON
PHAGOCYTOSIS IN ADULT BLOOD

Strain	History of Culture Tested	Normal Blood	Sulfanilamide* Blood
"McL"	1x in normal serum neopeptone	0 — 0%†	0 — 0%
	1x in sulf * serum neopeptone	0 — 0%	0 — 0%
"Aps"	1x in normal serum neopeptone	112 — 36%	506 — 88%
	1x in sulf serum neopeptone	334 — 54%	420 — 82%
"Gal"	1x in normal serum neopeptone	306 — 50%	592 — 72%
	1x in sulf serum neopeptone	372 — 62%	701 — 78%

* Sulfanilamide concentration = 10 mg per cent

† Fifty cells counted

(The blood used in this experiment contained antibody for strains "Aps" and "Gal" but not for strain "McL", cf, the phagocytosis by normal blood of the normally grown strains)

Table III shows that phagocytosis is most marked when Streptococci are grown in sulfanilamide media and are added to blood which contains both sulfanilamide and antibacterial antibody. This experiment also illustrates the variation of strains in their susceptibility to sulfanilamide.

TABLE IV

THE PROGRESSIVE ATTENUATION OF BACTERIAL VIRULENCE BY SUBCULTIVATION IN
SULFANILAMIDE MEDIA

Phagocytosis*	Blood Sulfanilamide	History of Inoculum	Bacteria Killed by 0.25 Cc Blood
0 — 0%	0 mg %	15x in normal serum neopeptone	0
	10 mg %	1x in sulf † serum neopeptone	40
	10 mg %	3x in sulf serum neopeptone	300
	10 mg %	5x in sulf serum neopeptone	3,000
	10 mg %	15x in sulf serum neopeptone	6,000
	0 mg %	14x in sulf serum neopeptone, then 1x in normal serum neopeptone	0

* Twenty-five cells counted. This blood contains no demonstrable antibody for the test strain.

† Sulfanilamide concentration of 10 mg per cent

(4) *Bactericidal Tests*—Table IV shows the results obtained from an experiment in which it is demonstrated that sulfanilamide grown organisms are killed by defibrinated human blood which contains no demonstrable antibacterial antibody. This bactericidal effect is shown to be due to an attenuation of bacterial virulence by sulfanilamide, because the only variable in the experiment is the progressive subcultivation of the Streptococci in sulfanilamide media, and the bacteria from the fifth subculture are killed in significantly larger numbers than the organisms from the first subculture. This effect of sulfanilamide also disappears as soon as the bacteria are cultivated in normal media again.

TABLE V

 THE DEMONSTRATION OF THE NECESSITY FOR BOTH ANTIBACTERIAL ANTIBODY AND
 SULFANILAMIDE FOR THE MAXIMAL BACTERICIDAL EFFECT

Exper No	Phagocytosis*	Blood Sulf	History of Inoculum	Bacteria Killed by 0.25 Cc
1	0 — 0%	0 mg %	3x in normal serum neopeptone	5
		10 mg %	3x in sulf † serum neopeptone	300
	124 — 60%	0 mg %	3x in normal serum neopeptone	50
		10 mg %	3x in sulf serum neopeptone	30,000
2	0 — 0%	0 mg %	3x in normal serum neopeptone	0
		5 mg %	3x in sulf serum neopeptone	1,300
	168 — 76%	5 mg %	3x in sulf serum neopeptone	130,000
3	210 — 88%	0 mg %	3x in normal serum neopeptone	13
		10 mg %	3x in sulf serum neopeptone	30,000

* Twenty-five cells counted

† Sulfanilamide concentration of 10 mg per cent

Table V shows the results obtained from a series of experiments which demonstrate that the combined action of sulfanilamide and antibacterial antibody is more effective than either one alone. Other similar experiments indicate that the effective level of antibody action is markedly lowered in the presence of sulfanilamide.

Experiments performed in human serum have failed to demonstrate any increase in the streptococidal power of the serum as a result of the addition of sulfanilamide or the use of sulfanilamide-grown organisms. It is concluded that sulfanilamide affects the Streptococci to render them more susceptible to the bactericidal action of defibrinated whole blood.

(5) *Clinical Observations*—A dramatic therapeutic response to sulfanilamide has occurred in the treatment of two types of acute hemolytic Streptococcus infections. The first type comprises those infections in which the patients have antibacterial antibody to their organisms at the time treatment is started, and the second type consists of those patients who have no antibacterial antibody and negative blood cultures with beginning localization of their infection by the process of inflammatory fixation. However, there is a third type of infection, in which the patient has a bacteremia with no antibacterial antibody, and sulfanilamide therapy alone has failed to sterilize the blood stream in these cases.

There are six cases of bacteremia without antibacterial antibody which have received sulfanilamide in sufficient dosage over a long enough period of time to evaluate adequately the sulfanilamide response in this type of infection. Three of these six patients died with continuously positive blood cultures on the second, third and fifth days, respectively, after sulfanilamide therapy was started. A fourth patient received only sulfanilamide and eventually recovered, but it was not apparent that the drug had dramatically influenced the course of his disease. The two remaining patients received sulfanilamide with no apparent improvement in the course of their bacteremia. Sterilization of the blood stream and subsequent recovery followed

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immediately upon the injection of antibacterial antibody by the method of immunotransfusion ¹⁵

TABLE VI

THE DEMONSTRATION OF THE RESISTANCE OF A STRAIN OF STREPTOCOCCUS TO THE EFFECT OF SULFANILAMIDE

Exper No	Phagocytosis*	Blood Sulf	History of Inoculum	Bacteria Killed by 0.25 Cc
1	0 — 0%	0 mg %	3x in normal serum neopeptone	5
		10 mg %	3x in sulf + serum neopeptone	2
2	168 — 88%	0 mg %	3x in normal serum neopeptone	500
		10 mg %	3x in sulf serum neopeptone	2,000

* Twenty-five cells counted

† Sulphanilamide concentration of 10 mg per cent

Table VI shows the result obtained from a bactericidal experiment, with a strain of Streptococcus isolated from a patient who died with Streptococcus bacteriemia, despite the fact that a blood sulfanilamide level of 9 mg per cent was maintained for three days prior to death. The experiment confirms the clinical observation that this strain of Streptococcus was relatively little affected by sulfanilamide and that antibacterial antibody was needed to achieve the streptococcidal effect. Tables VII and VIII are clinical summaries of the two patients with bacteriemia and no antibacterial antibody who required antibody in addition to sulfanilamide to sterilize the blood stream.

TABLE VII

CLINICAL SUMMARY OF A MALE, AGE 7, SUFFERING FROM BACTERIEMIA (STRAIN "MCL") WHO HAD NO ANTIBACTERIAL ANTIBODY, AND WHO REQUIRED ANTIBODY IN ADDITION TO SULFANILAMIDE TO EFFECT STERILIZATION

Days	Sulfanilamide Dosage	Blood Level	Transfusions	Blood Cultures	Remarks	W B C
1	2.4			Pos	Stuporous	5,000
2	2.4				Stuporous	
3	2.4				Stuporous	
4	2.4	7.7	Nonimmune 300 cc *		Stuporous	6,000
5	2.4			Pos	Stuporous	8,900
6	2.4				Stuporous	9,100
7	2.4	6.5		Pos	Stuporous	10,400
8	2.4	4.9	Immune 350 cc †		Stuporous	
9	2.4			Neg	Reactive	15,500
10	2.4				First abscess	21,200

* Phagocytic titer 0 — 0% (25 cells counted)

† Phagocytic titer 175 — 68% (25 cells counted)

COMMENT—Human virulent variants of hemolytic Streptococci are known to be resistant to spontaneous agglutination, resistant to phagocytosis, and resistant to the bactericidal power of human blood which contains no specific antibody ^{9, 10}. Streptococci which have been grown in media containing sulfanilamide have been shown to be spontaneously agglutinable, sus-

ceptible to phagocytosis, and killed by human blood that contains no specific antibody. These are the characteristics which serve to identify the attenuated or avirulent variants.^{9 10} Growth in sulfanilamide induces a physico-chemical alteration in the antigenic structure of hemolytic Streptococci which decreases the invasive capacity, or virulence, of the bacteria. These changes are strictly conditioned by the presence of the drug and are reversible upon withdrawal.

TABLE VIII

CLINICAL SUMMARY OF A FEMALE, AGE 20, SUFFERING FROM BACTERIEMIA, WHO HAD NO ANTIBACTERIAL ANTIBODY, AND WHO REQUIRED ANTIBODY IN ADDITION TO SULFANILAMIDE TO EFFECT STERILIZATION

Days	Sulfanilamide Dosage	Blood Level	Transfusions	Blood Cultures	Remarks
1	*			Pos	T 104° F, P 140
2	0.4				
3	6.0	11.0			Irrational
4	6.3	6.9	Nonimmune 350 cc †	Pos	T 103° F, P 120
5	6.3	10.9	Immune 500 cc ‡	Pos	
6	7.0	5.9	Immune Serum 260 cc	Neg	
7	0			Neg	T 99° F, P 110
8	0				
9	0				T 98.6° F, P 80

* Patient received 40 cc "prontosil" and was then changed to sulfanilamide by mouth.

† Phagocytic titer 0 — 0% (25 cells counted)

‡ Phagocytic titer 236 — 88% (25 cells counted)

Different strains of Streptococci vary in their susceptibility to this effect of sulfanilamide. Some strains are so altered by the drug that normal blood is bactericidal for these strains even in the absence of specific antibody. Other strains are affected so slightly that the bactericidal mechanism still depends upon the presence of antibacterial antibody for the streptococidal effect, but it is believed that the efficiency of the antibody is increased for organisms of this type which have been grown in sulfanilamide.

It has been found that patients with sustained bacteriemias and no antibacterial antibody are inadequately treated by the use of sulfanilamide alone. The experimental and clinical evidence indicates that effective therapy for this type of infection should consist of sulfanilamide and the intravenous injection of specific antibacterial antibody by the immunotransfusion technique.

CONCLUSIONS

(1) Sulfanilamide has been found to render human virulent strains of hemolytic Streptococci more susceptible to the bactericidal action of human blood, and this effect is reversible upon withdrawal of the drug.

(2) Antibacterial antibody is necessary in addition to sulfanilamide in the treatment of certain types of sustained hemolytic streptococcal bacteriemias.

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DISCUSSION OF THE PAPERS OF DOCTORS LOCKWOOD, LONG AND BLISS,
AND LYONS

DR DEAN LEWIS (Baltimore, Md) I am not a therapeutic optimist When Doctor Long began his experimental work with this drug, I waited rather anxiously for a case which would be a true test of the therapeutic efficacy of the drug I should ask Doctor McFee to say something about this case, for he may believe that the results would justify me in becoming a therapeutic optimist

The patient was operated upon in 1930 He had an otitis media, and subsequently a mastoidectomy was performed Chills and fever developed and the jugular vein was ligated because of thrombosis Pain developed in the right hip Blood cultures revealed a beta-hemolytic Streptococcus It is not necessary to give a detailed history In 1931, a suppurative arthritis of the right sacro-iliac joint developed An abscess was opened and 150 cc of thick pus removed No rough bone was felt In 1931, the patient was discharged from the hospital with a sinus Subsequently the right sacro-iliac joint was drained, the right wing of the ilium was removed, and a diagnosis of a chronic suppurative arthritis of the sacro-iliac joint made He did not improve rapidly and was sent to Rollier's clinic in Switzerland In 1936, an abscess beneath the right iliac muscle was drained Abscesses were also drained which were located in the deep muscles of the back After this long clinical course he came to the Johns Hopkins Hospital The Proteus organism and a Streptococcus were found Forty-eight hours after the first dose of sulfanilamide, the temperature became normal The character of the discharge from the 15 discharging sinuses changed and became thin and pink in color Within six months the boy had gained 62 pounds and the discharging sinuses had healed The patient has gone to a boys' camp in New Hampshire, and Doctor McFee told me this morning that the boy is now in New Orleans About all there is to remind one of his serious illness is a peculiar Charlie Chaplin-like walk This case furnishes a true test of the efficacy of this drug Ever since, I have been looking for a case of Streptococcic osteomyelitis, such as that which occurs in children and often runs the clinical course of suppurative arthritis, for I am quite certain that the clinical course would be modified by the drug, and it is quite possible that if a sequestrum

formed, it could be sterilized, and that the sequestium would then behave as a bone transplant

DR RICHARD H MILLER (Boston, Mass) As one may infer from what Doctor Lyons has said, we believe that the effect of the sulfanilamide is not dependent on any stimulation of the reticulo-endothelial system, or to any depreciation of toxin formation, but more probably to an alteration in the characteristics of the capsule of the Streptococcus

Furthermore, it seems to us that the effect of sulfanilamide is variable, depending on the blood culture and also depending on the presence, in some instances, of an anti-bacterial antibody Certainly, Doctor Lyons has been dramatically successful in saving some cases by employing blood transfusions in addition to sulfanilamide

One more minor practical point may be spread by you to professional colleagues in consultations and conversations That is, they must not allow themselves to have a false idea of security because they are employing sulfanilamide All the ordinary measures of surgery, in addition to the use of this drug, must be used

I should like to add one other point which brings me, I am afraid, into a little disagreement with Doctor Long, because I was going to say that we are quite against the use of sulfanilamide in any ambulatory cases I had it in my mind to say that we would not advocate its use except in hospitalized patients, where we could make, at the necessary intervals, the proper blood examinations, determination of the red and white count, and, if necessary, the condition of the phagocytes and perhaps the blood level of the sulfanilamide itself

DR EVARTS A GRAHAM (St Louis, Mo) There are just two points that I should like to comment upon in regard to this symposium

One is that I think perhaps all of the emphasis should not be placed on the therapeutic value of sulfanilamide If we will recall the first experiments made with this drug by Domagk, we will recall that he found that this agent was much more effective in the prevention of Streptococcus peritonitis than it was in the cure of the disease after it had been produced

As practical surgeons, I think that this point deserves a considerable amount of emphasis and so I am driving it home, if necessary For several months now, we have been using it at the Barnes Hospital almost as a routine in cases in which we might have occasion to predict a flare-up of a streptococcal infection by operation We have used sulfanilamide as a prophylactic measure beginning two days before the operation

I have had the opportunity to observe what seemed to me rather striking results in the fact that in a considerable number of cases of chronic empyema, in which it was necessary to perform rather an extensive operation, with large incisions, going in the neighborhood of or passing through a sinus of the chest, already infected, it was possible by the use of sulfanilamide as a prophylactic measure to have these wounds healed by primary intention Again, I have seen this same event occur in other parts of the body where it was probable that a severe streptococcal infection would take place as the result of an operation opening into an already infected field It would seem to me that this principle might have a bearing upon problems which confront neurologic surgeons in brain abscesses, often and perhaps to an even greater extent, a bearing upon many of the problems which the gynecologist faces or the obstetrician, if you will, in dealing with latent infections of the pelvis in which subsequent operations are necessarily performed We think we have

noted much better healing after intrathoracic operations, other than chronic empyemas, as the result of the prophylactic use of this agent, notably, for instance, in lobectomies

The dose has been something which has bothered us. I don't know whether any of the speakers this afternoon would be able to enlighten us on what might be regarded as a suitable prophylactic dose. We have tried empirically several doses and several methods of administration. Now we ordinarily, because of our ignorance and lack of knowing what might be best, give the drug in a ratio of a twentieth of a gram per kilogram of body weight parenterally, and we give about 500 cc slowly, subcutaneously, to the patient while he is on the operating table. We begin the administration of the drug preferably about two days before the operation and we continue it particularly while the patient is on the operating table.

There is just one other point I wish to mention and then I am through. Until last summer, I had never had the good fortune to see a patient with an acute suppurative pylephlebitis following an acute appendicitis recover. Others, of course, have seen such patients recover but I have never had that good fortune. It happened, however, that inside of six weeks, two patients developed this condition in the Baines Hospital, both of them with jaundice, both of them with chills and high fever. In desperation, we thought we would take a chance on sulfanilamide. I couldn't be very optimistic about it but, at any rate, we used sulfanilamide on these two patients and they both made a rapid and uneventful recovery.

DR ALLEN O WHIPPLE (New York, N. Y.) I wish to pay tribute, to Doctor Lockwood for the work that he has been carrying on during the last two years, and I would like to say that he illustrates the possibilities of a resident contributing fundamentally and soundly to scientific work and at the same time developing into an excellent surgeon. I also would like to emphasize the importance of an adequately supervised bacteriologic laboratory working in the surgical department, headed by a man who understands both surgery and bacteriology.

I think Doctor Meleney deserves a great deal of credit for the stimulus he has given, not only to us at the College of Physicians and Surgeons, but to the other clinicians in advancing this type of work.

As an example of the teamwork that can be developed Doctor Lockwood was one of a committee, at the Presbyterian Hospital, which supervised and reviewed all of the cases in which the administration of sulfanilamide was advised. The patient was not given sulfanilamide until one or more members of that committee had seen the case and advised its employment. As a result of that, a great deal of the helter-skelter and hit-or-miss therapy that has been carried out in a good many places with sulfanilamide was, I think, avoided.

This is a drug that carries with it possibilities for harm as well as for good, and in large hospitals, particularly, the work should be carefully supervised by both the medical and the surgical and the laboratory groups.

DR J. SHELTON HORSLEY (Richmond, Va.) I would like to refer to a cure by sulfanilamide of a case of Streptococcic peritonitis by Dr. John S. Horsley, Jr. The diagnosis was apparently appendicitis, but at operation the appendix appeared grossly normal. There was a large amount of free, turbid fluid which contained Streptococci and other evidences of peritonitis. The case was treated with sulfanilamide and the recovery was dramatic.

As regards preparatory treatment, sulfanilamide is apparently not directly

bactericidal, but it seems to affect the capsule of the bacteria, rendering them more vulnerable to the phagocytes. In the Colibactragen of Steinberg, we have an excellent preparation for the prevention of peritonitis. Undoubtedly, it has a great deal of merit, and as Steinberg has shown, it is, of course, not a bactericidal preparation but it increases the number of phagocytes, and stimulates their activity and their effectiveness. If this Colibactragen is used in established peritonitis, it has no effect. The toxins of peritonitis seem to depress the phagocytes after peritonitis has been established. Sulfanilamide in some way seems beneficial both as a preventive and as a curative agent.

DR VERNON C DAVID (Chicago, Ill.) As far as I know, there has been no suggestion made that virus diseases may be beneficially influenced by sulfanilamide. I would like to report several experiences, in principle, that seemed to indicate that there are some beneficial effects from the use of sulfanilamide in lymphogranuloma inguinale. Any of you who have had experience with the treatment of that disease know that it is highly resistant to treatment of any type that we know of.

A few months ago, I saw a patient who had a very well developed rectal infection with lymphogranuloma inguinale, and for whom all the known methods of treatment had been employed, such as ammonium and potassium tartrate, the luetic treatment, *etc*, none of which had resulted in any improvement.

Doctor Knight, of Chicago, suggested, after the failure of any therapeutic benefit from any of these methods, that we might try sulfanilamide. "Well," I said, "I think it's all right to use," and promptly forgot about it. About two months later, a doctor from the town in which this man lived wrote me and said that he had examined the patient, whom I had advised to have a colostomy performed for a lymphogranulomatous infection of his rectum, who, as far as he could discover by examination, was well. At my request the patient returned, and on examination showed very little evidence of the disease.

Now, that would be only suggestive, but at that time we had in the hospital a boy with a deep, progressive infection of the ischiorectal fossa which had involved the adductor region and which was accompanied by a secondary hemorrhage, for whom deep roentgenotherapy, tatar emetic and antiluetic treatment, treatment Frei antigen and everything else had been administered that we could think of, without any result whatsoever. Biopsy showed no carcinoma or tuberculosis. The Frei test was positive.

We therefore started this boy on sulfanilamide, giving him 20 gr., increasing it 20 gr. a day until he had 90 gr. a day for three days, then allowing him to rest for two or three days, and repeated this regimen seven different times. He immediately started to improve, and I had the pleasure of showing him to some of the men in this audience the other day, he is, apparently, entirely well.

Coincidentally with that, there have been about three or four other patients who have been treated the same way and all had evidenced marked improvement. I would suggest, in these very intractable cases and in the rather hopeless situation in instances of lymphogranuloma inguinale, it might be worth while to try this drug.

DR DAVID E ROBERTSON (Toronto, Canada) The use of sulfanilamide has become world wide, and one reads nothing but good results from its administration. There is no denying the fact that following its administration there have been brilliant and picturesque recoveries made. It is equally true

that the drug is apparently wholly ineffective in other cases, even in instances where a high level of concentration is maintained in the blood

One must remember that before the use or the knowledge of this drug existed, spontaneous recoveries did occur in streptococcal infections. I consider the drug is an agent that may be of the greatest use in the treatment of certain streptococcal and other infections, but it would be interesting to see a record in those cases in which it has failed to change the course of the disease

DR ERWIN R SCHMIDT (Madison, Wis) I would like to call attention to one phase of this subject. At our hospital, our anesthetists are extremely reluctant to put any people asleep who have had sulfanilamide and have had cyanosis.

They have a certain degree of anoxemia and in these cases where you have a short operation to perform, if you give them light anesthesia, such as nitrous oxide and oxygen, the chance for producing and increasing anoxemia is very definite

DR ARTHUR M SHIPLEY (Baltimore, Md) I would like to report one experience that has not been touched upon. The patient had a very active, localized pelvic inflammatory disease. I attempted to effect vaginal drainage. A short incision had only been made through the mucous membrane of the vaginal wall, when an alarming hemorrhage was encountered, which it took me three-quarters of an hour to control. I actually had to split the entire posterior vaginal wall. She was very cyanotic and the anesthetist was very much concerned during the whole procedure, although she was not half as frightened as I was. However, the patient recovered from the cyanosis, hemorrhage, operation and anesthetic.

The collection of pus, however, increased in the pelvis, so that later, it could be approached through a left McBurney incision. Her cyanosis had disappeared at the time of the second operation, and she had no unusual bleeding. The operation and drainage were accomplished without difficulty.

The relationship of intractable bleeding to the cyanosis, incident to the administration of sulfanilamide, has not been touched upon today and I would like to call attention to it.

DR RALPH R MELLON (Pittsburgh, Pa) I should like to inquire of Doctor Lyons relative to what he said about the mechanism or action of the drug, namely, acting on the organism and so altering the surface capsule as to permit it to become phagocytic. If that really is an adequate explanation of the mechanism, why is it that Levaditi and others have shown that if the drug is injected directly into the peritoneal cavity of mice, these mice are not saved, but if it is injected subcutaneously or orally, the mice are saved?

Furthermore, why is it possible, if this mechanism is correct, to add the drug in high concentrations to Streptococci in the test tube and then, the mice, being injected with these organisms, are still not saved even though pre-mobilization of the phagocytes have been brought about?

DR JOHN S LOCKWOOD (closing) As far as the practical application of sulfanilamide therapy in surgical infections is concerned, our own experience has been quite similar to that of Doctor Long, and I am inclined to subscribe to the principles that he presented so clearly. We have not used the very large initial doses which he recommends but there is certainly a good deal of rationale in so using the drug.

I do not think we will attempt, on this occasion, to unravel the differences

of opinion on the action of sulfanilamide which have been promulgated. Perhaps it is not surprising that there should be almost as many differences in the understanding of the action of the drug as there are people working with this material.

There are certain points, however, that I would like to bring up with respect to the situations in which the action of the drug is limited. We had a baby of 11 months with a primary Streptococcic peritonitis, who was treated with sulfanilamide and whose peritonitis cleared up very dramatically. However, during the course of intensive sulfanilamide therapy, this child developed a suppurative phlebitis of the saphenous vein, and out of the localized abscess which formed over it were cultivated perfectly normal, virulent-looking Streptococci. In addition, this child, whose initial septicemia had been cured, developed from that phlebitis a recurrent septicemia which continued in spite of continued drug therapy for many days. She eventually recovered.

It did seem, however, in that case and in a number of other instances, that the presence of an infected thrombus in a large vessel militates very strongly against satisfactory results with sulfanilamide in curing a bacteriemia.

In our own experience, it has been possible for us to believe that, in cases of bacteriemia which have failed to respond to the drug, there was a definite element of suppurative phlebitis. Perhaps it is because the drug does not get at the blood clot and the organisms in the clot or thrombus, or it may be for some other reason.

Doctor Lewis mentioned a very interesting patient with a very prolonged infection. We had, at the Presbyterian Hospital, a patient of Dr. Hugh Auchincloss', who had a very similar infection. In fact, these two children came down with the disease within about a week of each other and their cure was effected at just about the same time. This patient of ours had gone along for six years, during which time she had been in the hospital almost continuously. Her response was equally dramatic, perhaps more rapid because the extent of her disease was not quite so great as it was in Doctor Lewis' case.

Certainly, sulfanilamide has seemed to have no effect on localized Staphylococcic infections. However, reports in the literature and the limited experience of our own hospital have suggested that sulfanilamide may actually have a real place in treating invasive Staphylococcic infections where a high degree of localization with tissue break-down and pus formation have not occurred, factors which even with Streptococcic lesions are thought to interfere with the action of sulfanilamide.

Therefore, I think that in early cases of Staphylococcic osteomyelitis, bacteriemia, and in cases of Staphylococcic cellulitis where there is no localization, treatment with sulfanilamide in the same way as we are using it for Streptococcal infections is indicated and may possibly produce favorable results, whereas, it will fail to work in localized carbuncles and abscesses.

DR PERRIN H. LONG (closing). Sulfanilamide is so widely used that I cannot resist telling a story that I heard in the Johns Hopkins Hospital exactly a month ago.

A resident from one of the leading Boston hospitals had lunch with me. He said, "You know, the other night at staff meeting, our resident was going over the records and he said, 'Say, do you know what I think? I think we'd better just give everybody who comes to the hospital sulfanilamide and if they're not well in five days, then we'll do a physical examination.'"

I do not think we have gotten quite to that point, but we have come to

the conclusion that if a patient is severely ill and shows the clinical signs of infection which are responding to sulfanilamide, then it is better to treat the patient with sulfanilamide rather than to await the bacteriologic confirmation of the clinical diagnosis. If this is done, valuable time will not be lost and a fatality may be prevented. If, in such an instance, the bacteriologic results do not confirm the clinical impression, then sulfanilamide could be discontinued and no harm will be done.

In the Johns Hopkins Hospital we have had only one patient, who had adequate sulfanilamide therapy, die. I think in our Streptococcal infections this is the only case who should have gotten well and who did not.

We believe that this is probably due to our high dosage and our insistence on high blood levels. We can show in mice, which have no natural resistance to speak of (many of them have none at all), that there is a definite relation between the height of the blood level and recovery from Streptococcal infections. In the clinic, inadequately treated patients, in our experience, do very badly.

Recently, there was a very interesting article that appeared in the Canadian Journal of Medical Research. It has nothing to do with bacteria but it has to do with tomato plants. Doctor Marshall told me about this paper yesterday coming up on the train, in which it was shown that minute amounts of sulfanilamide stimulated the growth of tomato plants. It might turn out that very minute amounts of sulfanilamide might stimulate the growth of bacteria because sulfanilamide in tomato plants behaves very much as a plant hormone does. So I cannot insist too much on our idea of high sulfanilamide blood levels until the infection is under control, and once under control, then we believe that you should discontinue the drug as quickly as possible with safety.

DR CHAMP LYONS (closing). In answer to Doctor Mellon's question I do not believe Streptococcal infections in mice are entirely comparable to Streptococcal infections in man, for a number of reasons which cannot be gone into at this time. The discrepancy which he mentioned I believe is due to the fact that Streptococci must be grown continuously for a period of time in the presence of sulfanilamide to maintain this attenuation of virulence, and that in diminishing or low concentrations of the drug, they revert immediately to the virulent phase.

I should like to say, in reply to Doctor Robertson's remark that many of his patients have died, that I believe it likely that they are patients who had no antibody. There are two things, in addition, which I should like to bring up. First of all, patients who receive blood transfusions while they are receiving sulfanilamide therapy should have a determination of their compatibility made with their blood containing sulfanilamide. We have had a few instances in which it looked as if the sulfanilamide in the blood had altered the compatibility of the blood for receiving transfusions.

The second point is that sulfanilamide therapy used for prophylactic purposes requires that the Streptococci must grow in it for a period of time before it can exert its prophylactic effect. A year or so ago, a report was made on the use of sulfanilamide in the treatment of 16 patients with colon bacillus pyelitis. Four of these patients developed an acute hemolytic Streptococcus sore throat during treatment. The subsequent course of the disease was benign and they recovered, but normal Streptococci were able to implant themselves on a body tissue already saturated with sulfanilamide. After growing in the presence of the drug, they were altered and killed.

TREATMENT OF HEMATOGENOUS NEPHRITIS WITH SULFANILAMIDE*

CASE REPORT

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THE FOLLOWING case, and the accompanying chart which contains exhaustive clinical details, emphasize the value of sulfanilamide in complicated renal infections following postoperative septicemia, and demonstrate the importance of chemical and bacteriologic studies in order to direct the treatment intelligently

Case Report—BUI No 26884 W E M, male, age 59, entered the Brady Urological Institute April 26, 1938, complaining of difficulty and frequency of urination, and, recently, complete retention. His general condition was excellent. Examination of the chest and abdomen was negative. Blood pressure 130/95, pulse 88. The peripheral vessels were moderately sclerotic. The genitalia were negative. Rectal examination revealed a considerably enlarged, smooth, elastic prostate with areas of induration in the lateral lobes and also in the seminal vesicles. Prostatic secretion, obtained by massage, contained pus cells. *Diagnosis* Benign prostatic hypertrophy and prostatitis. A posterior cysto-urethroscope entered easily and recovered 20 cc residual urine. The capacity of the bladder was 300 cc. Rounded median and lateral lobes were present and partially obscured the trigone which was moderately hypertrophied. The ureteral orifices appeared normal.

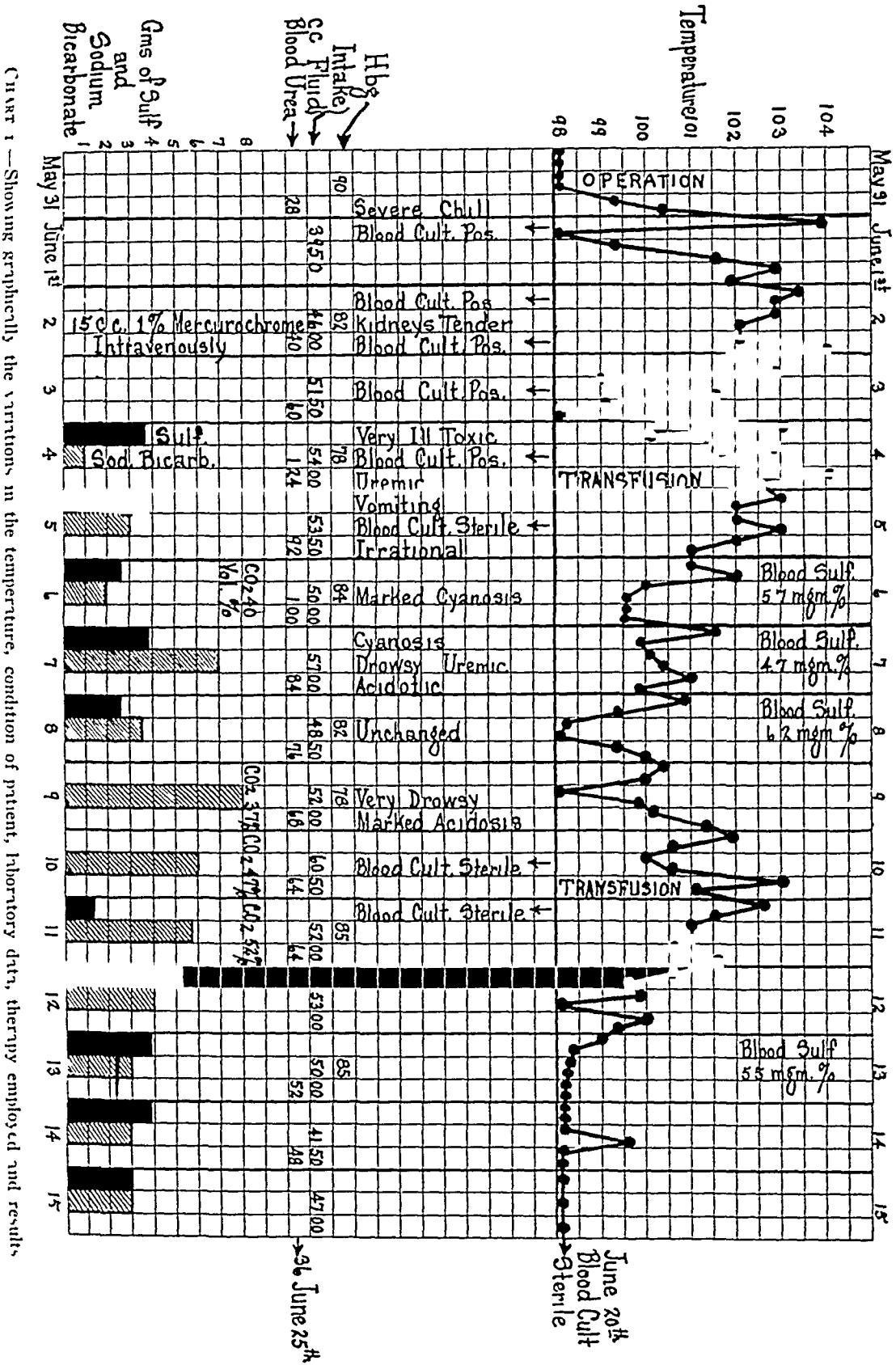
The patient left the hospital for four weeks and returned May 27, 1938, for operation. At the time of readmission, the retention of urine was complete and, on catheterization, 1,050 cc were recovered. On the following day, catheterization was again necessary, 900 cc urine being removed. Cultures of the urine were reported sterile, but on May 28, 1938, the temperature rose to 101.4° F. The phthalein test showed an appearance time of six minutes, and half-hour excretions of 50, 12, 8 and 5 per cent, making a total of 78 per cent in two hours. Blood urea 28 mg, hemoglobin 90 per cent, white blood cells 7,600. The urine was clear, acid, specific gravity 1.010, no albumin or sugar, no white or red blood cells or bacteria were found on microscopic examination. On May 29, 1938, the temperature did not go over 100° F, and on the following day the patient was afebrile. Culture of the urine was again reported sterile.

Operation—May 31, 1938. Dr. Hugh H. Young. Under spinal anesthesia, the prostate was exposed through a curved perineal incision. An incision through the apex of the prostate on the right side was made for introduction of the tractor, and the lateral and median lobes were easily enucleated through bilateral capsular incisions. The hemorrhage was slight, but the Davis bag and tube were inserted for hemostasis and drainage. After approximating the levator ani muscles with plain catgut, the skin was closed with interrupted sutures of silk, and drainage was provided through the right-angle of the wound. There was no appreciable change in the blood pressure or pulse during the operation. Microscopic examination of the tissue removed showed benign prostatic hypertrophy and chronic prostatitis.

Subsequent Course—The patient was returned to the ward in good condition, but by midnight the temperature had risen to 101.4° F. Numerous clinical and laboratory

* Part of this work was made possible by a grant from the Labor Foundation

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data, together with the temperature curve, are detailed in Chart 1, on which is recorded the condition of the patient from day to day, the hemoglobin, amount of fluid taken by mouth, subcutaneously or intravenously, the dosage of sulfanilamide and sodium bicarbonate, the blood sulfanilamide in milligrams per cent, the carbon dioxide combining power, and the blood transfusions. Many of these data, therefore, have been omitted from the daily comments on the patient's progress. The chart graphically shows the onset of septicemia and suppurative nephritis, sterilization of the blood by chemotherapy, but persistence of the nephritis, culminating in uremia, the excellent effect of sulfanilamide, until the patient developed acidosis and a marked drop in hemoglobin, which required blood transfusions.

June 1 The patient had a chill and rise of temperature to 103.8° F at 4 A M. A blood culture was taken and subsequently showed a massive growth of *B. Aerobacter aerogenes* (*B. lactis aerogenes*). The temperature dropped to normal, but by 8 P M it had reached 102.8° F. The Davis hemostatic bag and tube were then removed.

June 2 At 8 A M the temperature was 102.8° F. Blood cultures taken at this time again showed *B. Aerobacter*. The abdomen was distended and both kidneys were markedly tender. The blood urea had risen to 40 mg. In order to combat the septicemia the patient was given an intravenous injection of 15 cc of 1 per cent mercurochrome at 11 A M. There was the usual "postinjection" rise of temperature, which reached 104° F at 8 P M, followed by a rapid drop, which reached 99° F at 8 A M the following day. Cultures taken on June 2 and 3 were still positive, but the number of colonies had greatly diminished.

June 4 The patient appeared desperately ill. He was toxic, drowsy, hiccoughing and perspiring profusely. The temperature was 104.2° F. There was little secretion of urine and the blood urea was 124 mg. Blood cultures taken at 10 A M were reported positive. At 9 P M the patient was given sulfanilamide (Prontylin) 3.6 Gm by mouth, and sodium bicarbonate, 1 Gm. His condition was so desperate that a transfusion of 600 cc of citrated blood was given, as shown in the chart, which records all the laboratory reports.

June 5 The patient continued toxic, drowsy, nauseated and unresponsive. The temperature was 103° F. The blood urea was still elevated (92 mg). A blood culture taken at 9 30 A M was reported sterile. At 11 A M the patient was given sulfanilamide, Gm 1.3, and sodium bicarbonate, Gm 1, in water (150 cc). This dosage was repeated at 4 30 and 10 P M.

June 6 The patient was somewhat better, there was more urinary drainage and less tenderness over the kidneys. Blood urea 100 mg, hemoglobin 84 per cent. The free blood sulfanilamide was 57 mg per cent. The patient was markedly cyanotic. The CO₂ combining power at 9 30 A M was 40 volumes per cent. The patient was given sulfanilamide, Gm 2.6, and sodium bicarbonate, Gm 2.

June 7 The patient remained very drowsy and showed clinical evidence of acidosis. The free blood sulfanilamide was 47 mg per cent. The blood urea was 84 mg. The temperature varied from 98.8° to 101.6° F. Although the blood cultures had been reported sterile, it was apparent from the continued high blood urea and marked evidence of uremia that a renal infection (pyelonephritis) was present and that continuation of sulfanilamide therapy was imperative. The patient was given sulfanilamide, Gm 3.8, and, on account of the acidosis, sodium bicarbonate, Gm 7, in divided doses. The free blood sulfanilamide was 47 mg per cent. The urinary output increased to a good volume.

June 8 The temperature ranged from normal to 100.8° F. The blood urea dropped slightly to 76 mg. The blood sulfanilamide was 62 mg per cent, but the patient was very cyanotic, obviously in marked acidosis, restless with deep respirations, nevertheless, on account of the evident suppurative nephritis, sulfanilamide was continued, Gm 2.6, and sodium bicarbonate, Gm 3.6.

June 9 The patient continued restless and drowsy, acidotic, but took fluids well.

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The blood urea was 68 mg. The CO₂ combining power had dropped to 37 volumes per cent. On this account the sulfanilamide was discontinued. The patient was given sodium bicarbonate, Gm 8, in divided doses.

June 10 The patient showed marked anemia (Hb 64) and was given 600 cc citrated blood, and sodium bicarbonate, Gm 6. No sulfanilamide was given. The temperature rose to 103° F, but the blood culture remained sterile.

June 11 The patient was improved. The hemoglobin was 85 per cent and the blood urea 64 mg. There was no evidence of acidosis, but the temperature rose to 102.6° F, and it was apparent that additional sulfanilamide was indicated to combat the renal infection. The patient was given sulfanilamide, Gm 13, and on the following day the blood sulfanilamide was 53 mg per cent. This was accompanied by a drop in temperature, the highest being 100.6° F. After this the patient was given intensive treatment with sulfanilamide and the temperature rapidly approached normal, as shown in the chart.

June 12 The patient was given sulfanilamide, Gm 38, and sodium bicarbonate, Gm 4.

June 13 Sulfanilamide, Gm 38, and sodium bicarbonate, Gm 3, were given. The blood sulfanilamide was 55 mg per cent. The blood urea was 52 mg.

June 14 The temperature was normal and the patient felt fine. The tenderness over the kidneys had disappeared. The blood urea was 48 mg. The patient was given sulfanilamide, Gm 38, and sodium bicarbonate, Gm 3.

June 15 The temperature, pulse and respirations were normal. The patient sat up in bed, and his appetite was excellent, but regardless of his general condition it was considered unsafe to discontinue the sulfanilamide. He was given sulfanilamide, Gm 3, and sodium bicarbonate, Gm 3.

June 16 Inasmuch as the patient continued to improve, sulfanilamide was discontinued. By June 21, the blood urea had become normal, blood pressure 130/70, hemoglobin 85 per cent. The patient's general condition was excellent and he voided 2,950 cc of urine in 24 hours.

June 27 to July 8 The patient continued to improve. The perineal wound, treated frequently with 2 per cent mercurochrome, had healed and he voided about 4,000 cc of urine daily. Blood urea 36 mg, hemoglobin 85 per cent. The phthalein test showed excellent renal function, which was the same total as on admission, but cultures of the urine still showed the presence of *B. Aerobacter aerogenes* and a few white blood cells. The patient left the hospital on July 8, 1938. The operative result was excellent and he was voiding normally. On September 25 he was reported to be well.

DISCUSSION —Clinically, the patient appeared to have completely recovered from his renal infection, but it was not determined whether the infection was entirely vesical or also involved the kidney. It is evident that a massive blood stream infection developed shortly after operation, as a result either of bacteria involved in the chronic prostatitis, or the catheterization before operation which was followed by fever. Not infrequently, after urethral instrumentation, cystoscopy or even simple catheterization, a so-called "urethral chill," followed by high temperature and positive blood cultures, occurs. As a rule, the blood stream infection is transitory, but in our case it is apparent that a pyelonephritis developed rapidly, and presented the most serious problem during the postoperative course. The rapid increase in blood urea, the development of acidosis and the steady drop in hemoglobin presented very serious problems which required the most painstaking laboratory studies to determine just what form of therapy was indicated from day to day. The use of sulfanilamide was followed by a rapid sterilization of the blood, but the infection of the kidneys persisted, as

shown by the continuation of the temperature, the progressive increase in the blood urea, the development of pronounced uremia and drop in hemoglobin. To combat this, the continuation of an adequate dosage of sulfanilamide was necessary, but this precipitated an acidosis which finally made it necessary to discontinue the sulfanilamide and greatly increase the ingestion of sodium bicarbonate. When the acidosis was reduced, the continuation of the fever and high blood urea made it imperative to resume the sulfanilamide therapy which, fortunately, was followed by a progressive drop of the temperature to normal and was not accompanied by acidosis. While undergoing intensive treatment with sulfanilamide, the patient went on to rapid recovery, with a return of the blood urea and hemoglobin to normal. Without the assistance of the laboratory to determine the blood sulfanilamide content and the CO_2 combining power, as well as the various methods of estimating renal function, this case could, probably, not have been brought to a successful termination.

We are indebted to the Winthrop Chemical Company for the sulfanilamide (Prontylm) used in this case, and for a grant for research.

THE TREATMENT OF INTRAPERITONEAL ABSCESS ARISING FROM APPENDICITIS

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EARLY in 1936, an abrupt change occurred at the University of Virginia Hospital in the method of treatment of abscess resulting from appendicitis. Although for several years the practice had been followed of allowing poorly localized intraperitoneal infections to become definite abscesses before operating, the conservative treatment of cases of appendicitis presenting a mass began at this time to be prolonged. It was apparent that many of these cases, as shown by others, could be discharged from the hospital practically well without the necessity of operating. These cases were instructed to return for interval removal of the appendix just as is the common practice when abscesses have been drained surgically. After two years of the practice it was thought wise to determine by an appraisal of the actual results whether in our hands expectant treatment of an appendiceal mass had justified itself. The results of the appraisal seem to confirm the clinical impression that this method is the method of choice.

MATERIAL—The material on which this analysis is based consists of all cases of acute appendicitis admitted to the hospital during the five year period 1933–1937, a total of 1,069 cases. Only those cases are included which, after appendectomy, were reported by the pathologist as showing microscopic changes of acute disease, or that without operation presented a clinical picture to be defined. This resulted in the exclusion of all cases of frank or doubtful chronic appendicitis. In 240 of the 1,069 cases, infection had spread beyond the appendix as described below. One hundred and eighty-one cases of the 240 were diagnosed as intraperitoneal abscess.

Classification—In agreement with Schullinger's¹ implications, it is felt that lack of clarity and uniformity of definition of the pathologic stages of appendicitis is partly responsible for widely differing opinions on treatment following perforation. For this reason a careful attempt has been made to define the grades of appendicitis as classified in the present study. Whenever possible, an individual case has been placed in the less advanced group. For instance, many cases of perforation, which recovered promptly following early operation, are classified as simple acute appendicitis, inasmuch as they presented no evidence of an established peritonitis.^{2, 3} Although more careful study has been given to the hospital records of the 240 cases with extra-appendiceal peritoneal infection, the operator's note, the pathologist's report and the temperature chart have been reviewed in the remaining 829 histories.

The cases have been grouped in three classifications (Table I)

Group I—Simple Acute Appendicitis In the cases in this group operation was performed immediately on admission to the hospital. They include (a) Cases which presented on microscopic examination acute or subacute appendicitis without perforation, (b) cases presenting perforation or gangrene of the appendix, in which the postoperative course demonstrated no independent peritoneal infection, and (c) cases presenting perforation at operation, in which the appendix was completely separated from the general peritoneal cavity by being enveloped in the omentum.

Group II—Appendicitis With Abscess This group includes (a) Cases that presented an abscess at operation, and (b) unoperated cases, which on admission presented a characteristic clinical picture, *ie*, a typical history, definite sepsis, localized tenderness and the outline of a mass in the right lower quadrant.

Although it may well be pointed out that the diagnosis of appendicitis was not proven in these latter cases, yet the fact that the masses disappeared under conservative treatment with accompanying disappearance of the signs of sepsis argues strongly against their having been confused with other less common causes of right lower quadrant tumefaction. Assuming that all the masses on which diagnoses were based were the result of appendicitis, a doubt remains as to their all being true abscesses. Many may well have represented a diffuse inflammatory reaction agglutinating loops of bowel or a mass of omentum surrounding the diseased appendix. Some observers^{4, 5} assume with no definite proof that any mass which disappears gradually without operation is *ipso facto* not an abscess. Others^{6, 7} take the point of view, which seems more reasonable to us, that the line between abscess and nonabscess cannot be clearly drawn from clinical criteria. Whereas, doubt as to the presence of pus is unavoidable, it will be seen as the argument proceeds that the question is practically unimportant, since the choice of treatment must depend on the clinical findings, and the results of treatment are of significance only as they refer to the clinical findings. With the implied reservation that true abscess may not always be present, the term will be used to designate the clinical class as defined above.

Group III—Appendicitis With Diffuse Peritonitis This group includes cases presenting clinical evidence of peritonitis extending beyond the right lower quadrant.

No attempt has been made to define the extent more accurately, inasmuch as on clinical and operative findings sharper definition is often impossible. In this group is found a small proportion in which appendicitis has not been definitely proven as the cause of peritonitis. Three or four cases of clinical general peritonitis have been excluded because of atypical history or of some other possible source of peritonitis. In many of the cases included in this group, localization of the infection to single abscesses occurred, these cases thereafter presented a problem similar to those of Group II.

METHODS OF TREATMENT—Five programs of treatment have been recognized in the cases of extra-appendiceal involvement (Table I).

Immediate Operation Forced—Cases are included under this heading in which immediate operation was decided upon, not because of the stage of the abscess or the accepted current practice, but because of unmistakable indications for surgical intervention.

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In the abscess group, two cases presented with acute intestinal obstruction and one with a subcutaneous communicating abscess close to rupture. These three cases obviously have no bearing on the problem of conservative versus operative treatment of abscess and will be no further considered except as they affect the mortality of the series.

Immediate Operation Elective—Operations in this group were performed on admission, particularly in the earlier years, on the basis of what we then considered established surgical principles. In the abscess group, they represent cases presenting well localized masses of some days' standing.

A few cases, especially those of the later years, represent instances of failure to diagnose abscess preoperatively. The term "immediate," as applied in the abscess group, does not imply an emergency procedure, but all operations were done within 24 hours of admission to the hospital.

TABLE I

INCIDENCE OF CHOICE OF THERAPEUTIC PROCEDURE BY YEARS											
Group I		Group II					Group III				
Simple		Abscess					Diffuse Peritonitis				
Year	Acute Appendicitis	<hr/>					<hr/>				
		Immediate Operation		Conservative Treatment Begun			Immediate Operation		Conservative Treatment Begun		
				<hr/>					<hr/>		
		Operation			Operation			Operation			
		Elec-		Elec-		No	Elec-		Elec-		No
		Forced	tive	tive	Forced	Opera-	Forced	tive	tive	Forced	Opera-
1933	202	2	39	3	2	0	0	9	4	2	1
1934	128	0	25	7	1	3	0	6	1	3	1
1935	164	0	23	3	3	3	0	4	1	3	0
1936	148	0	8	1	6	22	0	4	0	5	3
1937	187	1	3	1	5	20	0	7	0	4	1
<hr/>		<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
Totals	829	3	98	15	17	48	0	30	6	17	6

Conservative Treatment Begun, Operation Elective—In this group are included the cases presenting marked sepsis and evidence of incomplete localization of abscess, which, after a few days of conservative treatment, showed diminished sepsis and a sharply localized mass, and which were then operated upon as a matter of principle. It was believed at the time of treatment that these cases had shown maximum improvement and that, therefore, the optimum time for operation had arrived.

Conservative Treatment Begun, Operation Forced—This group includes cases presenting on admission evidence of either a well localized or a poorly localized abscess. Under conservative treatment the course of the disease took an unfavorable direction, and operation seemed indicated on unquestioned surgical principles.

These indications included acute intestinal obstruction, growth in size of the abscess, and threatened perforation of the abscess into the abdominal wall or the rectum, usually accompanied by increasing signs of sepsis. The written opinion of the operator was not taken alone as proof positive of the enforced nature of the operation, but his opinion was combined with the recorded changes in the patient's general and local condition.

Conservative Treatment Begun, No Operation—The cases in this group fulfilled the requirements for the diagnosis of abscess or diffuse peritonitis, and in none was operation performed before discharge

General Considerations of Treatment—Expectant treatment followed the Ochsner⁸ principles, modified by modern resources in maintaining physiologic balances. Nothing is allowed by mouth until the highest daily temperature comes to within about one and one-half degrees (Fahrenheit) of normal, the mass has definitely shrunk, and tenderness is slight or absent, when sips of water are permitted. Each day during the period of starvation at least 3,500 cc of water, containing about 100 Gm of glucose and 13 Gm of salt, are given intravenously to the average adult. If edema occurs, about 75 Gm of glucose are substituted for the salt. The serum protein and blood chlorides are watched after the first week, and the daily urine volume throughout. The actual intake of water and crystalloids is governed by these observations. Transfusions are given freely as indicated by anemia, hypoproteinemia or continued sepsis. Morphine is employed until favorable progress is definite. In the established abscess we see no value in Fowler's position. After water is started by mouth, other liquids may follow in a few hours and later a soft hospital diet, unless unfavorable symptoms intervene. Enemata are used as sparingly as possible and duodenal suction is employed for distention and vomiting. The patients are watched very closely for the signs that suggest an impending enforced operation. In general, the patient is discharged when the temperature goes no higher than 99.0° F, and the mass has lost all its tenderness and can be felt with difficulty or not at all. At this time the leukocyte count has usually approached, or reached, the normal level. As experience increases with the method of prolonged conservative treatment, the indications for forced operation are becoming more strict. Whereas, earlier a rise of temperature for a day or so might be interpreted as indicating a necessity for operation, now, moderate pyrexia must be accompanied by objective signs of spreading infection.⁷

Except for choice of incision, technical operative procedures have been uniform. Practically all operations have been performed under spinal anesthesia, except in small children. Two types of incision are used, the McBurney, and a short right midrectus with retraction of the muscle toward the right. The appendix is removed whenever a search is not contraindicated by the patient's general condition or, in a few instances, when it is judged the local peritoneal reaction should not be greatly disturbed. With the exception of not more than ten or 12 instances in this series, the peritoneal cavity has been drained only when actual granulation tissue is present. In perforated or gangrenous appendicitis the wound is frequently drained to the level of the peritoneum.

Postoperative care has also been uniform. All cases with peritoneal contamination, including the borderline cases placed in Group I, are treated for a few days by the methods used in nonoperative treatment.

Change in Method—The change in the preferential method of treating

abscess, from immediate operation in well localized cases or elective, delayed operation in those poorly localized, to nonoperative treatment in all cases if possible, forms the chief basis of comparison in the present study (Table I) It is seen that, during the years 1933-1935, only 22.3 per cent of abscess cases were treated by conservative measures at the outset, and only 6 per cent were carried through without operation. Most of the former were cases poorly localized on admission, and of the latter, cases in which the abscess disappeared suddenly by rupture into the bowel, cases that refused operation and cases in which contraindications to operation existed. By contrast, in the years 1936-1937, in 83.3 per cent of abscesses, conservative treatment was started, and 65 per cent were carried through without operation. A few cases are seen to have been treated by elective operation during these latter years, the majority of these were in the somewhat transitional year of 1936.

The distribution of choice of methods of treatment in the diffuse peritonitis group (Table I) indicates no corresponding change in policy. Throughout the five year period the preferential immediate treatment of diffuse peritonitis has been nonoperative, and deviations from this course have resulted from diagnostic difficulties and the varying nature of the material.

METHODS OF STATISTICAL ANALYSIS—*Statistical Validation*—No unqualified conclusion, based on a comparison, is expressed unless the actual difference is more than twice the standard error of the difference, a ratio which is generally accepted as indicating a high probability of significance. Those data in which statistical validation has not been attempted or in which its results show that no significance attaches to the differences presented, will be indicated in the text. For purposes of clarity, the various standard errors have been omitted from the tables.

Mortality—The data presented bear largely on the appraisal of the results of nonoperative treatment in abscess. There is presented in addition a survey of the percentage incidence of admission of cases of all three groups year by year and of the corresponding mortality rates, for the purpose of furnishing a background for the special group to be considered, and of indicating the grade of success which the service attains in the treatment of appendicitis as a whole.

Morbidity—The measures of morbidity employed in estimating the results of treatment are (1) Days of hospital stay, (2) days of fever, (3) days of duration of drainage, and (4) number of complications and sequelae. The first three of these have been calculated only on the surviving cases. The complications have been computed in both living and dead cases.

(1) **Hospital Days** These include the day of admission and the day of discharge.

In the few cases which were transferred from other services to the department of surgery, the hospital days were numbered from the date of consultation to the date of discharge from the hospital.

(2) **Days of Fever** Absence of fever has been strictly interpreted as representing the first day during which the mouth temperature did not

exceed 98.6° F at any of the four daily readings. If after a day or two of normal temperature, fever again appeared, these days were included as days of fever. Inasmuch as many patients during the last hospital day presented mouth temperature readings slightly over 98.6° F, the exact duration of fever is often unknown. This has been indicated by computing the percentage of patients in each group whose temperatures had not come down to a conventional, strictly normal level before discharge.

(3) Days of Drainage. The exact termination of drainage in the hospital is difficult to determine from the records, because of differing definitions of the term. There is opportunity for error in the averages computed, but the opportunity is equally distributed in each group studied and the errors should tend to cancel each other. The problem of lack of knowledge of the termination of drainage, when cases were discharged to the family physician for home care, has also been met by computing the percentage of cases draining on discharge and not reporting to the hospital outpatient department.

(4) Complications and Sequelae (Table VI). The recorded complications and sequelae, compiled from hospital notes and postmortem reports, have been divided into three categories: (1) Complications and sequelae directly related to appendicitis through the spread of infection to the peritoneum, the portal system or the wound, including abscess in the wound, the cecal gutter, the pelvis, the liver or the subphrenic area, intestinal obstruction during the acute phase of the disease or months later, paralytic ileus, fecal fistula and postoperative ventral hernia, (2) complications indirectly related to the disease, including pneumonia, pulmonary collapse, pleurisy, empyema, thrombophlebitis and suppurative parotitis, and (3) complications unrelated to appendicitis, such as diabetes, pregnancy, syphilis, fibromyoma uteri, etc. The combined number of complications under the first two headings was calculated per patient in each group studied.

Miscellaneous—In addition to the comparisons of mortality rates and morbidity factors, two closely related problems have been investigated: (1) The success of nonoperative treatment in the extreme age-groups as compared to that in the middle age-group, and (2) the apparent effect on the later history of the patient of the failure to remove the appendix, both when an abscess was drained and when no operation was performed.

TABLE II
INCIDENCE OF TYPES OF APPENDICITIS ENCOUNTERED BY YEARS
Appendicitis, Peritoneal Infection

Year	Simple Acute	Abscess	Diffuse Peritonitis	Total	Total
1933	202—76 5%	46—17 4%	16—6 1%	62—23 5%	264
1934	128—73 1%	36—20 6%	11—6 3%	47—26 9%	175
1935	164—80 4%	32—15 7%	8—3 9%	40—19 6%	204
1936	148—75 1%	37—18 8%	12—6 1%	49—24 8%	197
1937	187—81 7%	30—13 1%	12—5 2%	42—18 3%	229
Totals	829—77 5%	181—17 0%	59—5 5%	240—22 5%	1,069

RESULTS —*Mortality in General*—The distribution of diagnoses between simple and complicated appendicitis shows fluctuations from year to year (Table II) In interpreting these figures, the stringent requirements for cases to be included in Groups II and III, as already defined, must be remembered The apparently not unusual average incidence of appendicitis with extra-appendiceal infection (22.5 per cent) in this series must be interpreted as relatively high Although not statistically determined, it is believed that the inclusion of all perforated cases in these groups, under the definitions presented by many other authors, could easily raise this percentage to nearly 40 per cent of the total cases It is interesting that Stone,⁹ using the conventional division of appendiceal from extra-appendiceal infection, reported from this clinic, in 1935, an incidence of 38 per cent of perforated appendices

TABLE III
MORTALITY BY TYPES OF APPENDICITIS AND BY YEARS
Appendicitis Peritoneal Infection

Year	Simple Acute			Abscess			Diffuse Peritonitis			Total			Total		
	Cases	Deaths	Mortality Percentage	Cases	Deaths	Mortality Percentage	Cases	Deaths	Mortality Percentage	Cases	Deaths	Mortality Percentage	Cases	Deaths	Mortality Percentage
1933	202	0	0	46	1	2.2	16	7	43.8	62	8	12.9	264	8	3.0
1934	128	2	1.5	36	3	8.3	11	6	54.5	47	9	19.1	175	11	6.3
1935	164	0	0	32	1	3.1	8	2	25.0	40	3	7.5	204	3	1.4
1936	148	0	0	37	2	5.4	12	6	50.0	49	8	16.6	197	8	4.0
1937	187	0	0	30	2	6.6	12	3	25.0	42	5	11.9	229	5	2.2
Totals	829	2	0.24	181	9	5.0	59	24	40.6	240	33	13.7	1,069	35	3.27

The mortality rate for the entire group of 1,069 cases is 3.27 per cent (Table III), a figure that compares favorably with average statistics Two deaths occurred in the simple acute group (0.24 per cent), representing the hazards of any operative procedure One case died of a rapidly progressive pneumonia following pulmonary collapse on the fourth postoperative day, and the other of an overwhelming *Streptococcus* infection of the abdominal wall The mortality in the abscess group (5 per cent) is not far above the general average for this series In the diffuse peritonitis group, however, a high death rate (40.6 per cent) is to be noted This is, in large part, explained by the method of classification

Rather marked fluctuations (from 1.4 to 6.3 per cent) are seen in the yearly mortality These figures and the data on the yearly incidence of complicated appendicitis can be shown to have a high coefficient of correlation Direct variation of an almost linear character apparently occurs (Chart 1) An increase in the relative number of complicated cases is associated with a corresponding increase in the mortality rate for the year, and vice versa, independent of any change in methods of treatment The present analysis of this relationship only confirms an often previously noted correlation

Treatment of Abscess—The assembled data in the abscess group of 181 cases reveal interesting differences in mortality and morbidity following different therapeutic programs (Table IV) (No statistical computations have been made involving the first column, as indicated earlier) The differ-

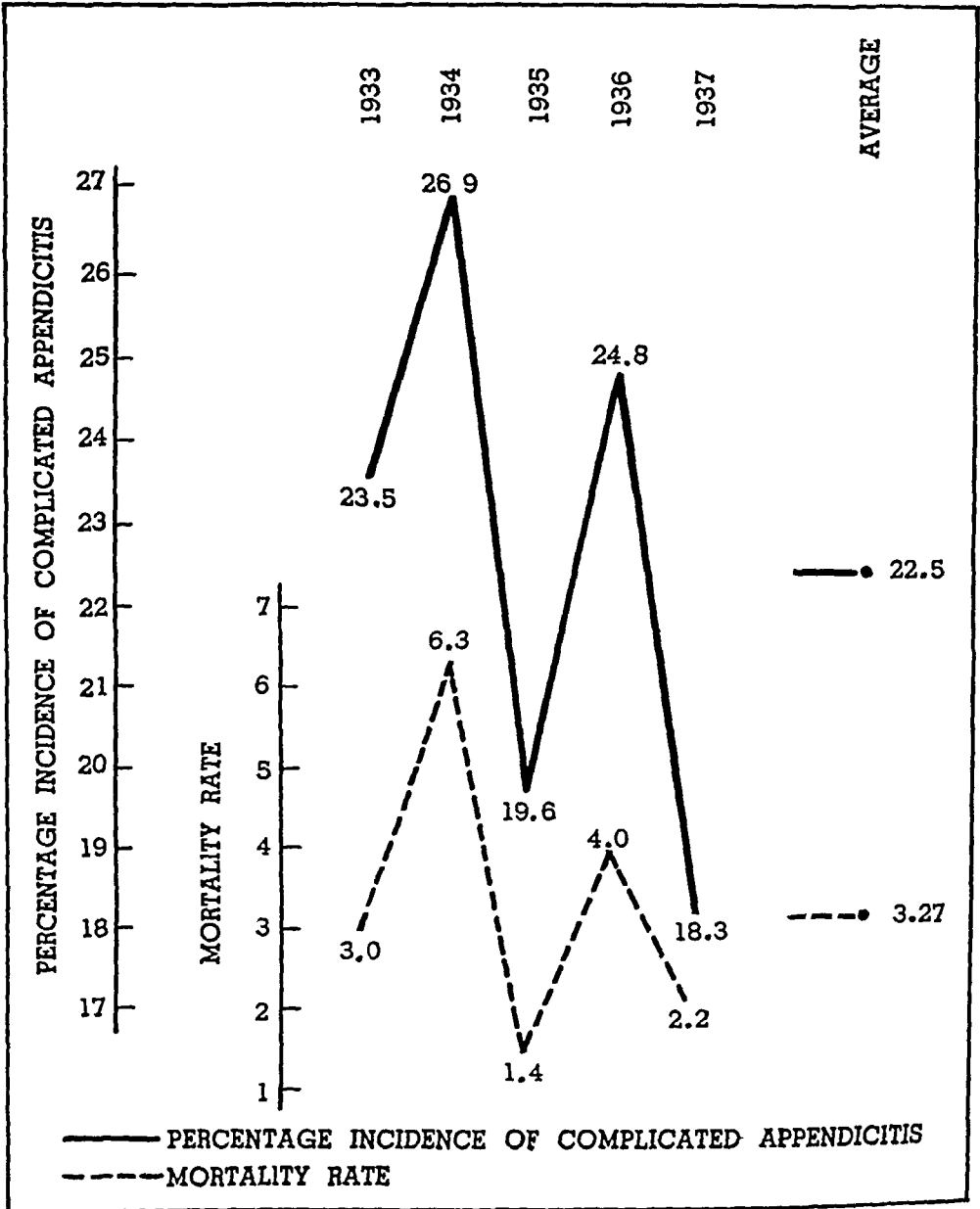


CHART 1—Correlation of yearly admission rate of complicated appendicitis *i.e.* with diffuse peritonitis and abscess, and the total yearly mortality from appendicitis

ences between all the mortality rates presented are statistically significant except for the comparison between the mortality rate of the group that underwent forced operation after initiation of conservative treatment and the mortality rates of the other groups. In other words, it can be stated with some positiveness, that the absence of mortality in the cases treated without

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TABLE IV
GROUP II ABSCESS

MORTALITY AND MORBIDITY FOLLOWING VARIOUS THERAPEUTIC PROCEDURES

	Immediate Operation		Conservative Treatment Begun		
			Operation		No Opera- tion
	Forced	Elective	Elective	Forced	
Data on Total Cases					
Number of cases	3	98	15	17	48
Complications per patient	1 66	63	60	94	0
Deaths	1	4	3	1	0
Mortality	33 3%	4 0%	20 0%	5 9%	0 0%
Data on Living Cases					
Number of cases	2	94	12	16	48
Average days in hospital	32	19 5	30 6	27 8	11 9
Average days of fever	29	17 7	25 2	25 8	9
Per cent of cases discharged with fever	0 0	46 9	16 6	56 0	31 2
Average days of drainage known	28 5	20 1	22 2	41 3	0
Per cent of cases in which date of termination of drainage is unknown	50 0	76 5	58 3	75 0	0 0

operation as compared with the mortality of 4 per cent in those treated by immediate elective operation and of 20 per cent in the small number treated by late elective operation, represents a significant difference in results associated with the differences in treatment. All of the morbidity factors, including complications (but excluding the percentages of unknown duration of fever and drainage) present statistically significant differences, with the exception of the unimportant comparison between late forced and late elective operation where the actual differences are small. One may state, therefore, that the absence of complications, the short hospital stay, the brief period of pyrexia and the absence of any period of drainage in the cases treated without operation represent real differences over the corresponding figures for forced late operation, and for either of the elective groups. For instance, the non-operative group shows no complications as against 0.63 complications per patient in the cases electively operated upon on admission, 11.9 days in the hospital as against 19.5 days, nine days of fever with 31.2 per cent unknown durations as against 17.7 days with 46.9 per cent unknown durations, and no days of drainage as against 20.1 days with 76.5 per cent unknown durations. It is perfectly unmistakable from this and further comparisons to be made in Table IV that *successful* conservative treatment is the most desirable method of treating this group of cases not only from the point of view of the prospect for recovery but also from the point of view of the severity of the patient's illness and the cost of hospitalization, to add nothing of the pain, odor, nuisance and expense associated with a drained abscess.

But, of course, this striking comparison does not present the whole story. If a group of cases is started on conservative treatment, a proportion will not do well and will require operation. In this series, of those so started, 60 per cent were successfully carried through, 18.8 per cent had elective operations after success was probable, and 21 per cent came to forced operation (Table VII). In view of the early behavior of cases in which operation was elected after marked improvement, it is probably fair to say that not more than a total of 25 per cent of conservative starts would be unsuccessful. A complete estimation of the results of conservative treatment must compare the combined results of successful and unsuccessful conservative treatment with those of all elective operations. Only in this way can one judge the propriety of initiating conservative treatment as the preferred program for appendicitis with abscess.

TABLE V
GROUP II ABSCESS

RESULTS FOLLOWING THE INITIATION OF CONSERVATIVE TREATMENT WITH SUCCESSFUL AND UNSUCCESSFUL GROUPS COMBINED, AS COMPARED TO RESULTS FOLLOWING ALL ELECTIVE OPERATIONS

	Conservative Treatment	
	No Operation and Operation Forced (Combined Columns 4 and 5, Table IV)	Elective Operation Immediate and Late (Combined Columns 2 and 3, Table IV)
Data on Total Cases		
Number of cases	65	113
Complications per patient	25	63
Deaths	1	7
Mortality	1.5%	6.2%
Data on Living Cases		
Number of cases	64	106
Average days in hospital	15.8	20.7
Average days of fever	13.2	15.9
Per cent of cases discharged with fever	37.5	45.3
Average days of drainage known	10.3	20.3
Per cent of cases in which date of termination of drainage is unknown	18.7	83.9

Such a comparison (Table V) reveals that the elective group suffers over twice as many complications as the combined nonoperative and forced delayed operative groups, remains in the hospital about one-third more days, is febrile almost 25 per cent longer, and drains practically twice as long. These figures in themselves, being all statistically significant comparisons, are striking evidence of the value of conservative treatment. The fact that the mortality is over four times as great in the elective operation group as in the conservative group must not be accepted too confidently, since the ratio of the difference to the standard error is just below two. However, the probability that the difference is not due to chance is high, and the figures, taken with the statis-

tically validated comparisons from the same table, are extremely suggestive. It may fairly be said that the results of the conservative regimen do not result in a higher mortality than the results shown by the electively operated cases, that probably the mortality is lower, and that the morbidity is strikingly less in all the measured factors. Inasmuch as the nonoperative cases leave the hospital in the possession of a diseased appendix, the possible later mortality and morbidity in this group must be considered a part of the problem and will so be considered below.

TABLE VI
TABULATION OF COMPLICATIONS AND SEQUELAE
DIVIDED ACCORDING TO METHODS OF TREATMENT

Nature of Complication or Sequela	Group II Abscess				
	Immediate Operation		Conservative Treatment Begun		
	Forced	Elective	Operation		No Opera- tion
			Elective	Forced	
Total Cases	3	98	15	17	48
Complications and Sequelae Directly Related to Appendicitis					
Residual abscess*	2	23	5	9	0
Subphrenic abscess	0	3	0	2	0
Gas gangrene	0	0	0	1	0
Obstruction in acute phase	1	2	0	0	0
Obstruction later	0	2	0	0	0
Paralytic ileus	0	13	1	1	0
Fecal fistula	0	6	1	1	0
Hernia, postoperative	0	3	0	0	0
Totals	3	52	7	14	0
Complications Indirectly Related to Appendicitis					
Pneumonia	1	3	1	0	0
Pulmonary collapse	0	0	0	1	0
Pleurisy, empyema	1	1	0	1	0
Thrombophlebitis	0	4	1	0	0
Parotitis	0	2	0	0	0
Total, both groups	5	62	9	16	0
Average complications per patient	1.66	63	60	94	0
Complications Unrelated to Appendicitis					
	1	9	2	2	6

* Includes abscess in wound, right lower quadrant, cecal gutter, pelvis, liver, etc

Nonoperative Treatment of Abscess in Relation to Age of Patient—It is, of course, a repeated surgical observation that patients at the extremes of life who suffer from appendicitis are sicker than those in the middle age-group. In this hospital, for instance, the mortality reported, in 1935, by Stone⁹ was for children 77 per cent as against 29 per cent for adults and

3.4 per cent for the entire material. Assuming the superiority of conservative treatment over operative treatment as a generally preferred program, it becomes important to determine whether age should influence the decision against an attempt at nonoperative handling.

TABLE VII

COMPARISON OF SUCCESS OF CONSERVATIVE TREATMENT OF ABSCESS IN DIFFERENT AGE-GROUPS

Age-Groups	Total	Conservative Treatment Begun			Deaths
		No Operation	Operation Forced	Operation Elective	
1-12 yrs	7	3-42 9%	3-42 9%	1-14 2%	0
13-54 yrs	57	38-66 7%	10-17 5%	9-15 7%	3
55 yrs plus	16	7-43 7%	4-25 0%	5-31 2%	1
Totals	80	48-60 0%	17-21 2%	15-18 8%	4

Computation of the number of cases successfully carried through non-operative treatment, in three age-groups (Table VII), indicates that at both extremes of life success is less apt to occur and forced operative measures are more frequent. Division of the group results in such small numbers in each subgroup that no positive statistical conclusion can be reached, and the apparent result must be accepted as being no more than suggestive. Certainly one should be particularly on the alert in children and the older patients for storm signals if conservative treatment is begun. It is interesting that of the seven children in whom expectant measures were employed, none died.

Later Course of Cases Discharged from the Hospital Without Removal of the Appendix—The conservative treatment of appendiceal masses in other hands has followed the experience described herein, 60 per cent or more of patients admitted to the hospital can be discharged without operation.^{4, 5, 6, 7, 10, 11} As already stated, the morbidity and mortality of this group resulting from retention of the damaged appendix must be charged against the method. It must be remembered, however, that a proportion of abscess cases subjected to operation (in this series 20.1 per cent) also leave the hospital carrying a diseased appendix. The disadvantage of this situation, when drainage is performed, is accepted by most surgeons as an undesirable but necessary part of an attempt to keep mortality low, and if the advantages, herein demonstrated, of conservative treatment as the preferred method are sufficiently impressive, the consequent failure to remove the appendix in the successfully treated cases must be accepted in the same sense. Just as in the case of patients discharged after drainage of abscesses without appendectomy, all patients conservatively treated are given a date for return for interval operation, are impressed as seriously as possible with the wisdom of this measure and are warned of the necessity for immediate return in the event of acute symptoms before the interval procedure is accomplished. The

date given for return varies from six weeks to three months after discharge, depending upon the original size of the abscess and the rate of subsidence of the process under conservative treatment

TABLE VIII
SUBSEQUENT COURSE IN ALL LIVING CASES FROM WHICH APPENDIX WAS
NOT REMOVED

Subsequent Course	Interval Removal	Readmitted Acute Appendicitis	No Further Recorded Trouble	Total
Drained	6	5	23	34
No operation	14	4	32	50
Totals	20	9	55	84
	23 8%	10 7%	65 5%	100%

A surprising condition revealed by this study is the small proportion of patients who take this advice (Table VIII). A little over one-sixth of the patients who have had abscesses drained have returned for interval appendectomy, and 28 per cent of those discharged after conservative treatment, a total return-rate of 23.8 per cent. Of those patients that had no operation, many more proportionally followed the surgeon's advice than of those that had been drained. The difference has no statistical significance, but it is interesting to speculate on the possibility that the unhappy hospital experience of the latter group might act as a deterrent to facing another operation. Certainly the patients treated conservatively with success, most of whom expected operation on first admission to the hospital, have no reason to fear another period of hospitalization.

Ten and seven-tenths per cent of the group discharged without appendectomy returned with an acute attack. Three of these nine patients had allowed the new attack to progress to rupture and abscess formation. None of the group that returned died, and none were seriously ill. One patient was treated conservatively for abscess twice and, impressed by the second attack, finally returned for interval removal.

The fate of the remaining 65.5 per cent, that have not returned to the hospital, is important. Homans¹² states that roughly one-fifth of those whose abscesses have been merely drained suffer a recurrence, and Haggard¹³ puts the figure at about one-half, as does Royster¹⁴ in quoting from Reschke. About 95 per cent of all the cases included in Groups II and III are admitted to the charity service, being sent most often by their physicians from rural districts. There is no other hospital to which these patients can go in the event of serious disease. It is, therefore, a fair assumption that the great majority of these patients have had no serious attack of appendicitis. Since it is obvious that many of them have been treated so recently that there may not have been time for serious trouble to develop, the data have been divided by groups of years (Table IX).

TABLE IX

SUBSEQUENT COURSE IN ALL LIVING CASES FROM WHICH APPENDIX WAS NOT REMOVED,
DIVIDED INTO YEAR-GROUPS

Year-Groups	No of Cases	Interval Operation	Readmitted With Acute Appendicitis	No Further Recorded Trouble
1933-1934	17	2 11 7%	4 23 5%	11 64 8%
1933-1935	25	2 8 0%	6 24 0%	17 68 0%
1936-1937	59	18 30 5%	3 5 1%	38 64 4%
Totals	84	20 23 8%	9 10 7%	55 65 5%

The figures in Table IX clearly suggest, without statistical proof, that there is no striking decrease in the number that have had further trouble in the last two years over that in the earlier years. Part of this result is due to the much larger proportion of cases that have returned for interval operation during the later period. Later figures may show a number returning with acute trouble that will approach the proportion of acute readmission in the earlier period. A longer time should elapse for a larger group of cases than the number now available before a complete follow-up would be entirely useful. Since the failure to follow advice has been shown to be unexpectedly prevalent, it is planned to communicate with the entire group of appendix carriers, urging return to the hospital for appendectomy. Possibly the development of a routine⁶ by which no patient would escape repeated invitations to follow this advice would help to justify the adoption of conservative treatment. In addition it would tend to protect the patients in the diamed group also from their own ignorance, fear or inertia.

The patients that have returned to the hospital for the interval removal of their appendices have spent an average of 81 days there. To furnish a complete picture of the economic aspect, this figure must be added to the 119 days (Table IV) spent during the period of conservative treatment, making a total of 200 days of hospitalization. The average stay for cases operated upon as an elective procedure is 207 days (Table V), but about 20 per cent of these cases must also face another hospital stay since the operation on that proportion has not included removal of the appendix. There therefore remains a slight economic advantage with the successfully treated conservative group insofar as hospital stay is concerned. The economic loss from two periods of illness is not easy to estimate. In general, the cases that leave the hospital after successful conservative treatment, however, have been ill a shorter time and are discharged in much better condition than those discharged after operation. Most of them go back to work almost immediately. Although total loss of time from work may be somewhat greater when interval appendectomy is added to the original illness, than if operation is performed at once, the difference cannot be sufficiently great alone to determine policy.

DISCUSSION —It is important to be certain that a suggestion to withhold operation in appendicitis be not misunderstood or adopted improperly. It need hardly be emphasized that the evidence presented has no bearing on early operation for acute appendicitis or on the expectant treatment of diffuse peritonitis. It refers only to the case in which a mass is already established. Furthermore, it offers no excuse whatever for the family physician or the surgeon to delay operation when there is no certainty that peritonitis is well localized. Finally, it is not intended to justify the nonoperative treatment even of a suitable case elsewhere than in a hospital, perhaps even than in a hospital so organized that a relatively mature resident surgeon is always available. The success herein shown, in the nonoperative treatment of abscess, must be assumed to be largely dependent on the possibility of ensuring complete general and gastro-intestinal rest, adequate maintenance of physiologic balances with frequent checks thereon, transfusions as may be indicated and, above all, close and constant observation.

During recent years a number of papers on appendicitis have presented the results of conservative treatment of an established mass^{4, 5, 6, 7, 10, 11, 15, 16, 17}. The data are usually confined to mortality rates, although in a few instances the incidence of complications and the length of hospital stay have been studied. A comparison of nonoperative treatment with operative treatment of abscess in the same clinic is rare. Comparisons of figures from different clinics are deceptive, not only because of differing methods of classification but also because of different ideologic and technical approaches to the disease.⁵

All authors whose reports upon the nonoperative treatment of abscess have been reviewed in a search of the recent literature¹⁹ have been satisfied with their results. The absolute figures for mortality agree in general with the figures presented herein, and the occasional records of the paucity of complications as well as of the surprisingly short hospital stay are also in agreement with our data. Sworn and Fitzgibbon's¹¹ study, especially, employing a classification of cases similar to ours and also indicating the group of cases in which conservative treatment fails, presents results convincingly parallel to ours. It may be noted that many unfavorably critical discussions of conservative treatment are based on theoretic considerations alone, presenting no data in support of arguments.¹⁸

As has been stated, there is some disagreement in the literature as to the condition that is treated, namely, whether or not an established abscess ever resolves spontaneously. This represents, of course, an unimportant distinction. The essential element is the localized mass following appendicitis for which conservative treatment is proposed, a mass which may or may not contain pus. The problem to be settled is whether such a mass is better treated by or without operation.

This study was undertaken, as has been said, to appraise the results of a method of treatment adopted on a clinical basis. The University of Virginia Hospital surgical staff is unanimous in the opinion that the data here presented

justify the continuation of this method under the local conditions. Success has been shown to be far greater than had been anticipated. It is felt that any case of appendicitis, at any age, which presents a mass is best handled by initiating expectant treatment in the absence of definite, immediate surgical indications, and that such treatment should continue so long as improvement continues. The sicker cases, that do badly without operation, probably belong to the type that would do badly with operation. The type that has shown adequate resistance to the infection clearly seems to have had a remarkably easier and less dangerous experience in our material when operation was withheld, than when operation was performed under what we used to consider favorable conditions. A paragraph from Love⁴ may well be quoted: "I feel sure that psychological reasons are a great deterrent to the adoption of expectant treatment. If a case treated on delayed lines ends fatally it is usually regarded as a tragedy, and all concerned may have lingering doubts in their minds as to whether immediate operation would have saved the patient. On the other hand, if the appendix is immediately removed and the patient succumbs, the general impression is that because immediate operation was performed everything possible was done, and the fatality is accepted philosophically."

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¹³ This survey comprises a list of 54 articles, detailed reference to which is omitted because of lack of space

DISCUSSION —DR FREDERICK A COLLIER (Ann Arbor, Mich) This paper has been most instructive to me, emphasizing as it does the value of the conservative treatment of abscesses, a point of view I have been approaching perhaps too slowly

The outstanding fact about appendicitis is the importance of removing the appendix early, while the infection is confined to the appendix or its vicinity Our main efforts should be expended toward bringing about this ideal treatment Unfortunately, we are called upon to treat the results of neglected cases or of poor treatment that result in diffuse peritonitis or abscess formation There is a diversity of opinion on the proper method of handling these two complications I think everyone now admits the importance of deferring operation long enough to restore the biochemical balance of the patient After this has been effected, many surgeons insist upon the immediate removal of the appendix or drainage of the abscess Others continue the Ochsner regimen, deferring operation until indications arise

In our clinic, for ten years, we have used the conservative method in the treatment of peritonitis, operating only if the patient does not improve or if the abscess develops In patients who come to the hospital with abscesses, we have usually drained the abscess after restoring the patient's biochemical balance During the past three years, we have been observing these patients with abscess for a longer time before operation, largely as a reflection of our conservative attitude toward peritonitis rather than due to any definite intellectual effort

About 60 per cent of the patients with peritonitis treated by the deferred operative method develop abscesses These abscesses are often large, filling the pelvis and bulging into the rectum or the lateral gutters, and we feel from our experience that these should be drained when their presence is obvious We have lost several patients in whom drainage of these large collections of pus was carried out too late

With the feasibility of conservative treatment of the mass around the appendix, be it single or multiple abscesses, or infiltrated omentum or intestine, I am in accord, due to our own small experience and to the observations of Doctor Lehman, and in this group, I propose to carry out the conservative treatment more as he has outlined I do think, however, we should draw a distinction between the large collections of pus resulting from the Ochsner treatment of diffuse peritonitis, and the well localized mass around the appendix, called an appendix abscess The collection of pus should be drained We urge the subsequent removal of all appendices that have been the cause of peritonitis or abscess

During the past four years, we have treated 574 patients with acute appendicitis and its complications, with a mortality of 19 per cent Of these, 496 had the disease limited to the appendix or its vicinity and these were treated without a death There were 32 patients with diffuse peritonitis, with a mortality of eight, or 25 per cent Of those dying, two were severe diabetics and one patient was moribund on admission Forty-six patients were admitted with abscesses and all but one were operated upon during their

stay Half of these were operated upon as soon as their general condition was satisfactory, usually within 24 hours The other half were operated upon in an average of one week after admission Three patients died, two of peritonitis and one of pneumonia It is possible that deferring operation longer might have led to a happier result

There is one great drawback to advocating any type of delay in the operative treatment of the complications of appendicitis It requires an effort of mind and the possession of surgical judgment, these are not always available The bare mention of conservatism in any connection with appendicitis is often misconstrued to mean medical treatment for all appendicitis

DR J SHELTON HORSLEY (Richmond, Va) Doctor Lehman's analysis of his cases is extremely interesting I have followed, during the last seven years, a somewhat different course of treatment It is necessary to have a basis for statistics of appendicitis, and that basis should be that every case of appendicitis treated, no matter by what means, must be included in the mortality rate A patient is just as dead who dies following the Ochsner treatment as one who dies after an operation

When you begin to split very fine clinical and pathologic hairs as to the difference in a stage of appendiceal inflammation, you are running into a great source of potential error Of course, with very excellent experience and good surgical judgment such as Doctor Lehman has, you can reduce the errors to a minimum, but one still has a potential field for them, no matter how careful one may be

During the past seven years, the surgical staff of St Elizabeth's Hospital, consisting of my two sons and myself, have adopted a general standard, which has proven quite satisfactory, partly because it is simple There have been three features which we have been using for a long time Immediate operation in all cases of acute appendicitis, the McBurney incision, and simple ligation of the stump of the appendix, but beginning about seven years ago, we combined five different features which I shall speak of later

TABLE I
DEATH RATE FROM APPENDICITIS PER 100,000
POPULATION IN VIRGINIA

Year	Deaths	Percentage per 100 000
1913	137	6.4
1920	194	8.4
1925	260	11.0
1930	267	11.0
1935	247	10.1

The highest death rate since 1913 was 12.9 per cent, in 1932

Table I shows the incidence of deaths from appendicitis As is well known, this death rate is increasing, at least it has been for the last 20 years Whether this is due to conservative treatment, to "freezing" it out, or to waiting, I do not know, but it just happens to come along that way while these procedures seem popular In Virginia, deaths show a very distinct rise from 6.4 per 100,000, in 1913, to 10.1 per 100,000, in 1935 The highest death rate since 1913 was 12.9 per cent, in 1932

APPENDICEAL ABSCESS

TABLE II

APPENDICECTOMIES AS THE MAIN PROCEDURE PERFORMED
AT ST ELIZABETH'S HOSPITAL

(January 1, 1931, to January 1, 1938)

	Cases	Deaths	Percentage
Acute appendicitis	494	3	0.607
Acute appendicitis with peritonitis	100	2	2.0
Subacute and chronic appendicitis	200	0	0
Carcinoma of appendix	1	0	0
	<hr/> 795	<hr/> 5	<hr/> 0.6

Table II represents our own statistics from January 1, 1931, to 1938, and I may say that we have had no deaths this year so far. We have tried to adopt a simple method of classifying the cases. We have what we call acute appendicitis, 494 cases with three deaths. We have acute appendicitis with peritonitis, in which we include, to make it as simple as possible, abscesses and spreading peritonitis as well, and in which we have 100 cases with two deaths. We have had 200 cases of subacute and chronic appendicitis, and one carcinoma of the appendix, with no deaths.

Of the five deaths, two were neglected cases when first seen. There was gangrenous bowel, which had to be resected at the time of operation, in one case, and an abscess of the tube on the left side which so involved the bowel that it had to be resected in another case. Then there was a patient, age 72, who had a retrocecal appendiceal abscess, that had been present for some weeks and which we thought was cancer of the cecum. The appendix was removed and the abscess drained. During convalescence, he developed a decompensating heart and pulmonary edema and died four days after operation. The fourth death was that of a man, age 50, who had a gangrenous appendix removed without draining and made a satisfactory recovery except for a fibrinous pleurisy, right side, ten days after the operation. That cleared up and the patient was about ready to leave the hospital when he died of a pulmonary embolus. The fifth death was in a very obese, alcoholic male, who developed paralytic ileus and uremia and died on the sixth day after the operation. Necropsy showed no peritonitis.

The routine procedures at our clinic are

(1) Immediate operation for acute appendicitis, as soon as the diagnosis is made, no matter what the stage of the disease.

(2) McBurney incision, gentle handling of the tissues, and always removal of the appendix. Removal of the appendix obviously saves morbidity and hospital expense, and reduces the mortality rate.

(3) Suction apparatus instead of sponging. Sponging presses sepsis into the areolar tissue. That is a very important point in technic. If you sponge the pus out with gauze on a sponge holder, you get out some pus but you also massage into the retroperitoneal tissues some of it.

(4) Physiologic rest of the affected colon and cecum, by avoiding proctoclysis and by administering intravenous dextrose or dextrose in salt solution or Ringer's solution, and using a Jutte or Levine tube in the stomach, also using a minimum of drainage. Physiologic rest is what we want, and by giving proctoclysis you are doing exactly the opposite thing. You are pouring into the colon and cecum, fluid which not only distends the bowel and tends to create peristalsis, but also increases the absorption from that region, because the right side of the bowel is the chief absorptive area for

fluids. In other words, you are working just as hard as you can, tissue that should be rested.

(5) The simple treatment of the stump of the appendix, merely ligating and bringing over a tag of peritoneum-covered fat to protect the stump from the drainage tube.

In every acute case, abscess or not, we operate at once and always remove the appendix. We have not failed to remove the appendix in a single one of these cases. But you should not do that unless you follow all five of those points.

H. E. Robertson, of the Mayo Clinic, has called attention to the fact that in every instance in which the appendix was removed, incidental to some other operation, and the patient died of something else, up to 21 days, he found a pocket of pus where the appendix stump had been buried. Simply tie a ligature around it, not clamping it, because that injures the tissues unnecessarily, just tying it tightly enough to cut through the mucosa, and let it roll up, cut off the appendix with an electric cautery, and disinfect the stump with carbolic. A tag of fat may be brought over by the ends of the ligature on the stump.

Let me repeat again that we have been doing all of these things for only seven years. We had been using McBurney's incision before for many years, but unless you are going to give the tissues physiologic rest, unless you are going to use a suction apparatus and not force the pus into the retro-peritoneal tissue, unless you are going to treat the stump of the appendix simply, these other things such as immediate operation and always removing the appendix should not be performed.

DR THOMAS G. ORR (Kansas City, Kans.) I have been very much interested in this report because we have been practicing practically the same method during the past three years. Any patient admitted to the hospital with a mass in the lower right quadrant of the abdomen, we allow to wait until we are sure that the mass is going to develop into a full-blown abscess before recommending drainage. About 50 per cent of our cases get well and go home without any operation. We are very careful to warn them to return at the end of three months for an interval appendicectomy. It is true that some of them will not come back, notwithstanding they have been advised it is their responsibility. Occasionally they return with another acute attack. We have had this happen in a number of instances, but do not consider that there is any more danger involved than that which attended their first attack.

There have been many different published ideas concerning the treatment of appendicitis. I had occasion a short time ago to review 12 different recent articles on the statistics of appendicitis with peritonitis, and I was surprised to find that the death rate varied from 14.3 up to 52 per cent. There is either a great deal of difference in appendices or there is something wrong with statistics.

We divide our cases into four groups. Those in which the disease is confined to the appendix, and those that have ruptured and have no distention, are operated upon at once. I believe distention is the crux of the whole situation. Those patients without distention who are operated upon and have their appendices removed have a very low death rate. The third group are those with masses in the right lower abdomen, which we allow to wait. We also postpone operation in the fourth group having general peritonitis.

After perforation and operation, an abscess occasionally develops in the pelvis. A large percentage of those masses will resolve without operation if given sufficient time.

DR ROSCOE R GRAHAM (Toronto, Can) I would like to express my personal thanks to Doctor Lehman for classifying the way in which he is studying appendicitis

One is lulled into a very false sense of security by a mortality of 3 per cent We have that, but at the same time, one analyzes the group in which the death occurs, as in the case that is perforated I have very little interest in reading a report on the treatment of appendicitis in which they have not very sharply differentiated perforated from nonperforated groups

In December, 1929, we lost two cases which presented masses, that were operated upon precipitately, without correction of the biochemical fault They both died of colonic bacteriemia We looked up our mortality on cases presenting masses, and it was 22 per cent We looked up our mortality on cases of perforated appendicitis, and it was 17 per cent The comment that was made to us was that we had better learn how to operate on appendicitis I do not believe that is the point I think that our management coincides very closely with Doctor Lehman's

There are two points I would like to make First, there are some people who are desperately ill and, as in some cases of perforated duodenal ulcer, one has been in error in determining why they are ill They are ill because of the biochemical balance that Doctor Coller has mentioned The patient comes in with a temperature of 105° F, cold to his elbows and cold to his knees, and a mass in the right iliac fossa That patient, when he has had his biochemical balance restored, is an unbelievable picture after 24 hours, if you have not experienced it

Sixty per cent of our cases have been discharged without operation We explain their responsibility and a very small percentage have not returned in three months Second, when you have full-blown abscess in the right lower quadrant, you are not operating for appendicitis You are operating for an intraperitoneal abscess and that is the same as an abscess any place else That means drainage

DR OWEN H WANGENSTEEN (Minneapolis, Minn) The method of treatment which Doctor Lehman has described has been a matter of routine in the surgical clinic at the University of Minnesota since 1931—a preliminary period of trial extending back to 1929 Since 1931, no appendiceal abscess has been operated upon primarily in our hospital Such cases are treated conservatively by the employment of suction applied to an inlying duodenal tube, even in the absence of distention, and by the administration of paroral fluids

I should like to offer a word of caution, however, concerning prolonged, expectant treatment in the patient with a very large abscess or rather in the patient whose abscess continues to be large As Doctor Lehman pointed out, a surprisingly large number of abscesses resorb completely without operative intervention—the patient then comes back for appendectomy in the interval If, however, a large abscess gives little evidence of resorption over a short period of observation, it should be incised For, apart from the possibility of intraperitoneal extension of the abscess by rupture, there is another hazard in large abscesses, namely, burrowing of the abscess into the mesentery with erosion of a blood vessel I have seen this complication, and as you can well believe, it is a disastrous occurrence

Subsidence of fever and *decrease* in the size of the abscess are the signs which indicate that it is safe to pursue a conservative regimen If fever continues unabated and a large abscess fails to diminish in size, incision and drainage are indicated

The advent of continuous gastric siphonage has, of course, extended the conservative plan of treating appendiceal abscesses outlined by the late A J Ochsner many years ago. I subscribe fully to what Doctor Horsley said concerning the avoidance of enemata. Evacuant enemata, as well as the administration of a barium enema for purposes of diagnosis, are hazardous in the presence of intraperitoneal suppuration. Many lives will be saved if house officers are instructed never to administer enemata when intraperitoneal suppuration is present or suspected.

DR ALLEN O WHIPPLE (New York City, N Y) With all the emphasis that has been laid upon the conservative treatment of peritoneal abscess, we have got to bear in mind the effect it has upon the general practitioner. During the past year, I have seen four patients, who have come in with either peritonitis or peritoneal abscess, and the reason the doctor gave was that he had read a good deal of literature recently about conservative treatment of appendicitis.

There is a danger we must bear in mind, if we continue to emphasize the conservative treatment. This is misunderstood by a great many of the general practitioners, who will find more advantage in treating their cases of appendicitis conservatively instead of having the cases operated upon during the time when the mortality, as is shown by two opposite methods of treatment, is exceedingly low.

DR HOWARD LILIENTHAL (New York City, N Y) What we should do is to try to influence the general practitioner so that not he, but the surgeon, shall decide whether or not an operation shall be performed. Surgery is not, strictly speaking, a science, it is only partly a science.

The most arresting part of this paper appears to me to be the urgent advice that practitioners of medicine should not take the responsibility of treating appendicitis without surgical counsel. After all, to call in a surgeon does not mean that an operation is inescapable. It simply means that the medical man will be reinforced by a surgical opinion. And that this will influence, but not necessarily persuade, the practitioner. This aspect of the subject should be frequently presented in medical literature.

DR EDWIN M MILLER (Chicago, Ill) I have been intensely interested for several years in the treatment of the type of case that Doctor Lehman has presented, and I have taken even a more conservative attitude than he seems to have followed. Ordinarily, these cases form a well recognized, clearly defined group, but, on the other hand, there is the occasional case where one is in doubt, even after a most careful examination, as to whether it falls into Group II or in one of the others.

When there is that matter of doubt, it may be cleared up by relaxing the patient very thoroughly under anesthesia. I have had the experience of having found a definitely palpable mass under anesthesia and leaving it alone. I have gone even further, and have opened the abdomen in an indefinite case and then have found a localized mass with the abdomen open, and left it alone.

I wish also to say that not every localized palpable mass, in a patient who gives a history which simulates that of a preceding acute attack of appendicitis, is the result of perforation of an appendix. I have had the experience of seeing a case where this was suspected, only to find upon entering the abdomen, not an appendiceal mass but an irreducible intussusception in which there had been an atypical history and atypical physical findings.

Not only that, but many of these localized, palpable masses do not occupy the right lower quadrant of the abdomen. Many times in our experience they have occupied the lower left quadrant and not infrequently, as has been said, they are confined to the pelvis.

DR FRANZ TOREK (Montclair, N. J.) I want to confine my remarks to one class of cases, namely, those with diffuse suppurative peritonitis. By "diffuse" I mean those that have extended well over to the left side, with free pus not only in the region of the perforated appendix but also in the pelvis and well over to the left side.

Those are rarely seen now, but between 30 and 40 years ago they were not rare. I reported on these cases in two publications, each covering 18 cases, so that, by 1908, I had recorded 36 cases with diffuse suppurative peritonitis. I mention them now because the way in which I treated them may perhaps be new to some of you.

The treatment consisted in a median incision from the pubis up to at least two inches above the umbilicus, letting the pus flow out through the wound, removing the appendix as quickly as possible, and then washing the entire peritoneal cavity with hot saline solution, first pouring it into the right side where the appendix was, then in the pelvis, then in the left side, and, if necessary, also higher up. The washing was accomplished by pouring from a flask or a pitcher and using the gloved hand to move the intestines from side to side, in order to reach all the places where pus might be found.

By 1908, as I say, I had operated upon 36 cases, but since then I have had only four cases, which is a proof that the diagnosis of appendicitis has been so much improved these later years that the extensively diffused cases of peritonitis are rarely seen.

An important thing is that in those cases, I did not drain. You may drain an abscess, and it ought to be drained, but if you have to deal with a diffuse peritoneal involvement, you had better make up your mind that it is impossible to drain the whole peritoneal cavity. The washing, therefore, had to be so thorough that the water finally ran back absolutely clear. The abdomen was closed without drainage. Only in a few cases in which I saw that the cecum was so nearly gangrenous that it was bound to perforate, did I insert a drain through a separate opening down to it. In those cases, after some time, pus and feces came out through the drain.

Another point is the closure of the wound. The incision was closed by simply taking through-and-through sutures without any attempt to coapt the separate layers. I did this in my first case, who was so extremely weak that I thought she would die soon after I got through, and that I must make haste to avoid having the patient die on the operating table. She, however, recovered, and since then I have continued to employ that same method of suture in all the cases of diffuse suppurative peritonitis.

The reason why I did not return to the customary suture, in layers, was to avoid spreading infection from the incision to freshly exposed muscle and fascia, as these tissues are not nearly as capable to resist infection as the peritoneum is.

The cases that I reported totaled 36, and there were six deaths. In the four subsequent ones, no deaths. So I had six deaths in 40 cases, a mortality of 15 per cent.

DR EDWIN P. LEHMAN (closing) I agree entirely with Doctor Coller in relation to the large abscesses. I have not had the experience that Doctor

Wangensteen reports, of rupture into a blood vessel, but I presume if we continue with this treatment, such an event may occur.

We believe that most of the large abscesses will do well with at least some delay in operation. In most instances a delay of three or four days will place the patient in considerably better condition for operation.

I know no statistics on appendicitis that are as good as those that have been presented by Doctor Horsley. Of course, as Doctor Colley has pointed out, the difficulty of comparison between clinics is very great. When Doctor Horsley was to present these statistics at our state meeting last fall, I looked up a group, approximately the size of the group that he has reported, limited to private cases, and I found that our mortality in the private group was not appreciably greater than that of the group he has presented.

We also have had the experience of having masses palpable by rectum disappear without operation in the same way that Doctor Orr reports.

We realize the danger of misconstruction of a proposal for conservative treatment in any phase of appendicitis and have, therefore, placed in a prominent position in the text of the present communication a clearly outlined statement of the type of case to which this treatment is limited, namely, the case with a demonstrable mass.

I agree that there is danger of missed diagnoses, and I presume also that they will be embraced in our experience. So far, we do not know of any diagnoses that have been missed by this method of treatment.

REGIONAL ENTERITIS

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REGIONAL enteritis, terminal ileitis, or nonspecific granuloma of the intestine is either occurring more frequently or is being recognized more often than in the past. A study of the literature on nonmalignant disease of the intestine gives the impression that many such lesions have been incorrectly diagnosed as tuberculosis.

Inflammatory intestinal lesions were recognized many decades ago. In 1806, a case was reported by Combe and Saunders in which three feet (90 cm) of the terminal ileum was involved. The description of this condition and the specimen strongly suggested that the process was nonspecific. In 1844, Abercrombie reported a lesion in the intestine of a child, age 13, which was apparently one of nonspecific ileitis. Another case of a similar nature was described by Braun, in 1909. The 14 cases reported by Crohn, Ginsberg and Oppenheimer, in 1932, gave the first classic description of what is known as "ileitis," "granuloma of the intestine," or "segmental enteritis." Others who have described inflammatory disease of the intestine are Tietze, Moschowitz, and Wilensky and Mock.

TABLE I

REGIONAL ENTERITIS

Brown and Pemberton's Series of 39 Cases

No. of cases	Segment Involved	Surgical Procedure	Results
2	Entire jejunum (1) Upper jejunum (1)	Exploration	Died 7 mos later
13	Ileum (1 to 8 segments)	Ileocolostomy	2 apparently well 11 slightly improved
2	Ileum and transverse colon	Ileosigmoidostomy	1 slightly improved 1 died 6 mos later
20	Ileum (17) Ileum and cecum (3)	Resection of ileum and cecum	16 well (2 to 6 yrs) 2 died later (cause unknown) 2 died postoperatively
2	Ileum and cecum (with fistula and abscess)	Drainage of abscess in right lower abdominal quadrant	Not traced

At the Mayo Clinic, several cases of so-called terminal ileitis have been observed in which the cecum and portions of the large intestine were also involved. In Crohn's original article he expressed the belief that this disease was confined to the ileum, but, in 1936, he and Rosenak reported a total of 60 cases, confirmed at operation, in nine of which there was involvement of some

portion of the colon Colp reported a case in which not only the terminal ileum but the cecum was also involved

In 1937, Pemberton and Brown collected 39 cases of nonspecific inflammatory disease of the intestine from the records of the Mayo Clinic In 36 of these cases the diagnosis was substantiated at operation (Table I) Since then 30 additional cases have been encountered at the clinic, which form the basis of the present report Twenty-one of these 30 patients were seen during a period of nine months It seems logical to infer from this, therefore, that the condition is occurring, or is being recognized, with greater frequency than previously

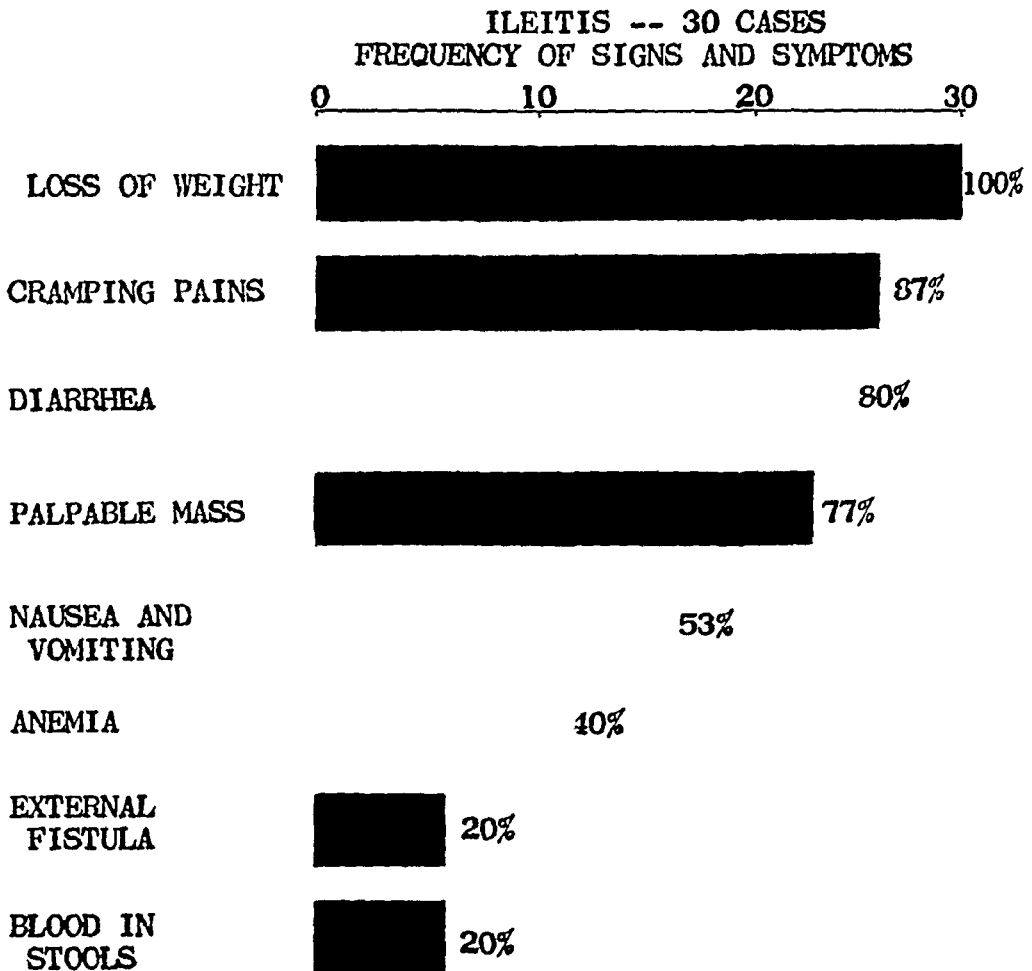


FIG 1—Frequency of signs and symptoms

Figure 1 graphically represents the signs and symptoms of the disease from the standpoint of frequency The chief subjective symptoms were intermittent cramping pain and diarrhea In each of the 30 cases there had been a moderate to marked loss of body weight The clinical history would lead one to believe that this reduction in weight was due to the patients' fear of eating rather than to the disease itself since the majority of them complained of cramps and pain soon after the ingestion of food On physical examination

a mass was present either in the pelvis or right lower abdominal quadrant in all except seven of the 30 cases. The rope-like character of the lesion was often manifest as a firm sausage-shaped tumor. In 16 cases there was a history of nausea and vomiting.

Marked anemia is frequently associated with disease, and particularly carcinoma, of the ileocecal region, but in these 30 cases of regional enteritis, anemia was present in only 12, and then only to a moderate degree, even though the enteric disease in some instances involved both the cecum and terminal ileum. The leukocyte count as a rule was slightly increased. Six patients gave a history of having passed blood by rectum, bleeding probably occurs more often in association with nonspecific enteritis than this statement would indicate, but is not noticed. A fistula of the external type was present in six cases, in three instances operation having been performed following a diagnosis of acute appendicitis. In some of the instances in which there had been a previous operation, mention of an indurated cecum or plastic exudate over the surface of the terminal ileum was made. In three cases fistulae of the internal type were present, one patient had a fistula between the ileum and urinary bladder and two a fistula between the ileum and lower part of the sigmoid.

In 23 cases, there was a definite history of remission of symptoms lasting from two to four weeks. Previous treatment had been instituted in 22 of the 30 cases, 13 patients had undergone appendectomy, and nine had been treated on the assumption that their difficulty was amebic dysentery.

The clinical history in each of these 30 cases strongly suggested regional enteritis and in each case this suspicion was substantiated roentgenologically. None of the patients had a history suggestive of active pulmonary tuberculosis and, roentgenologically, there was no evidence of pulmonary disease.

Surgical treatment was undertaken in all of the 30 cases. Single stage resection was performed in ten cases, ileocolostomy with subsequent resection in ten, and ileocolostomy alone in the remaining ten. In those cases in which ileocolostomy was the only surgical procedure, the patients were advised to return for resection of the diseased segment of bowel, but possibly because of improvement, they have not complied up to this date. It is of interest that all except three of these ten patients have the same symptoms as before surgical intervention but to a lesser degree. Eight of them have gained 15 to 20 pounds (6.8 to 9 Kg.). In the 20 cases in which single or two stage resection was employed, all symptoms completely subsided except in four cases in which a slight tendency to diarrhea remained (four to six stools daily).

In this series of 30 cases, upon whom 40 operations were performed, there were four deaths: one from pulmonary embolism, one from peritonitis, one from obstruction, and one from pneumonia. The fact that there was but a single death following the ten primary resections might lend credence to the belief that this procedure should be employed more often. My reason for performing primary resection in this group of cases was either that the patient appeared to be in good condition or that multiple external fistulae were pres-

ent In the latter instance many loops of intestine were found to be adherent in the right iliac fossa and, in order to become properly oriented in performing the operation, it was necessary, in my judgment, to mobilize the coils of intestine in this region en masse, which made a single stage resection imperative In all cases of resection a temporary stoma of the Witzel type was established at a point in the ileum about 24 to 30 inches (60 to 75 cm) proximal to the anastomosis This procedure has proved of great value in preventing distention due to the accumulation of intestinal gases The enterostomy tube is removed as a rule on the twelfth postoperative day and this is followed by spontaneous closure

It is my impression that, in its earliest stage, regional enteritis consists of enlargement of the mesenteric lymph nodes and ulceration of the mucosa Brief mention of two cases will tend to substantiate this opinion

Case 1—Female, age 29, came to the clinic because of intermittent attacks of severe cramping pain in the right lower abdominal quadrant These attacks had begun two months previously Her family physician, who had been in attendance during many of the attacks, reported having found moderate tenderness in the right lower quadrant, moderate elevation of the leukocyte count, a temperature of 102° F, and diarrhea consisting of three to five stools per day, unaccompanied by the presence of blood At the clinic, physical and laboratory examinations failed to reveal evidence of the disease, the patient apparently being in a period of remission Roentgenologic studies of the gastrointestinal tract, however, revealed a defect in the terminal ileum

Operation—On opening the abdomen no abnormality could be detected in the terminal portion of the ileum The small intestine and colon were then examined carefully but the lesion described by the roentgenologist could not be found The lymph nodes adjacent to the terminal portion of the ileum were slightly enlarged Two months after this exploratory operation the attacks recurred with increasing severity, and three months after the surgical intervention a second operation was undertaken, at which the distal portion of the ileum was found to be markedly thickened and covered by a thick, grayish, plastic exudate One stage resection was performed and satisfactory recovery followed

Case 2—Female, age 24, came to the clinic complaining of diarrhea, fever and acute abdominal pain which had occurred intermittently during the preceding six weeks, however, she had not consulted a physician Physical examination revealed no abnormal finding Other investigations did not show anything significant except that the roentgenologist reported the presence of a filling defect in the terminal portion of the ileum At operation, however, careful examination of the small intestine and cecum did not reveal the presence of a tumor or other abnormality The patient succumbed to pneumonia 12 days postoperatively At necropsy, the terminal ileum was grossly normal, but when the intestine was opened an ulceration 5 cm in diameter was found

The question is Should not these two cases be classified as instances of early regional enteritis or terminal ileitis?

In a third and similar case, in which there was no evidence of disease of the terminal portion of the ileum by direct visualization or palpation, the ileum was transilluminated by the use of a Cameron cold light, which was placed along the lateral surface of the intestine Such lesions as ulcerations or polypi can be visualized quite clearly in this manner, when by such measures as palpation no abnormality can be detected, further use of transillumina-

tion is suggested as an aid in determining the presence or absence of lesions in hollow abdominal organs

An analysis of the entire series of 69 proved cases of regional enteritis, in which the diagnosis was made and the patients were treated at the clinic, would lead one to the inevitable conclusion that the treatment of choice is radical removal of the involved intestine (Table II)

TABLE II
SURGICAL RESULTS IN 69 CASES OF REGIONAL ENTERITIS

No of Cases	Surgical Procedure	Results
25	Ileocolostomy	5 well, or have only mild symptoms 20 obtained slight or no improvement, or were worse
40	Resection	4 died postoperatively 2 died after dismissal (cause unknown) 34 well 6 mos to 6 yrs
2	Closed as exploration (condition too extensive for resection)	Died 7 mos postoperatively
2	Drainage of abscess	Fistula 8 mos later Fistula 1 yr later
—		
Total 69		

Cases have been reported in which spontaneous cure evidently occurred without resection, for example A colleague informed me recently of an operation undertaken upon a young woman for the purpose of removing an acutely diseased appendix Exploration revealed a so-called chronic appendix Appendicectomy was performed In the terminal ileum, about 10 cm from the ileocecal juncture, there was a definite thickened area covered by a thick, gray, plastic exudate The process apparently involved the entire circumference of the ileum The mesentery adjacent to the segment of diseased bowel contained many enlarged nodes Omentum was used to cover the affected portion of ileum and the abdomen was closed Nine months have passed since appendicectomy was performed in this case and meanwhile the symptoms have gradually subsided This case is mentioned as an example of the exception rather than the rule

Segmental enteritis is an inflammatory disease which has great tendency to progress, as is evinced by the fact that unless radical excision is employed, further spread of the process occurs, often involving the site of an anastomosis and thus necessitating another radical procedure Several such cases have been reported A case in point is appended

Case Report—Female, age 12, was admitted to the clinic because of an illness of two and one-half years' duration, which was characterized by fever, chills, cramping lower abdominal pain, diarrhea and vomiting For periods of a month or more the child was without symptoms Her growth had apparently been markedly impaired Examination revealed the presence of a diseased terminal ileum, the defect appeared

roentgenologically to involve about 30 cm of the intestine. Ileocolostomy was performed and the patient was advised to return in three months for resection of the diseased intestinal segment. Following the short-circuiting operation the symptoms decreased in severity and there was a marked gain in weight. Fourteen months after ileocolostomy the patient returned for reexamination. She appeared to be in good health. Meanwhile the stools had been loose occasionally but only mild attacks of cramping lower abdominal pain had occurred intermittently. At this time the defect in the terminal portion of the ileum appeared roentgenologically to be more extensive than at the previous visit. The mother of the child refused to have surgical intervention undertaken.

Experience in similar cases would lead one to believe that this patient will in the near future have symptoms of obstruction because of encroachment of the progressive inflammatory process on the ileocolonic stoma.

The cause of regional enteritis has not yet been explained. Some observers are inclined to think that an allergic tendency is responsible for it. Bohn has reported a case which is suggestive. A boy, age 9, complained of symptoms such as frequently accompany regional enteritis. He was hospitalized and given a liquid diet. Each afternoon his temperature became elevated to from 103° to 105° F. By a process of elimination it was discovered that when milk was not present in his diet, his temperature was not above 99° or 100° F, but that when the use of milk was resumed there was marked elevation of the temperature and associated cramping pain of much more violent character than during the period when milk was excluded. This case is at least interesting.

The consensus at present seems to place the cause of regional enteritis on an infectious basis. Pumphrey, however, has studied the enlarged lymph nodes as well as the segments of diseased bowel removed in many of the cases mentioned in this report. First, he attempted to prove the presence or absence of tubercle bacilli. Guinea-pigs were inoculated but none of them developed tuberculosis. Cultures were taken, using various media, but he was unable to detect any constancy of organisms. Many of the organisms that were recovered were cross-agglutinated with the patient's serum, but positive results were not obtained. Organisms recovered from the diseased intestinal wall and from the enlarged lymph nodes were injected intravenously into rabbits without producing visible lesions. Attempts were made to culture fungi from the lymph nodes and the affected tissues in three cases but the presence of pathogenic fungi could not be demonstrated.

SUMMARY AND CONCLUSIONS

A total of 69 patients with regional enteritis have been treated at the clinic.

Regional enteritis is apparently increasing in frequency, or the disease is being recognized more often than formerly.

Rational treatment at the present consists in resection of the diseased segment of intestine. A short-circuiting operation such as ileocolostomy often affords temporary relief and apparently, in isolated instances, the procedure may produce subsidence of all symptoms. A two stage operation seems the

procedure of choice So-called spontaneous cures, however, are occasionally recorded

Ulceration of the mucosa and enlargement of the mesenteric lymph nodes may be the beginning of regional enteritis, and transillumination of the intestine may prove to be an aid in locating such early lesions

The etiology of regional enteritis is unknown Studies of specimens which have been removed have failed to reveal a specific Bacterium as the cause of the disease A case is mentioned in which an allergic phenomenon was recorded

DISCUSSION —DR HORACE BINNEY (Boston, Mass) I do not feel that I can discuss the subject as a whole, which Doctor Dixon has presented so interestingly, because my experience is quite limited However, as concerns the treatment, I think it would be of interest to present to you a case in which I carried out a procedure which perhaps is not according to Hoyle, but which, under the circumstances, seemed to be the best thing to do and the result seems to indicate that I used correct judgment in employing it

The patient was a boy, age 19, who, four years ago, came under my care, with the usual history of attacks of appendicitis, the earlier ones subsiding and then having an appendicectomy, followed by the formation of a fecal fistula in the scar That was operated upon but the fistula broke out again He came then under my care again I felt it probably was a case of tuberculosis of the idiocaecal region At that time he had a fistula, a palpable mass, and some obstructive symptoms—a griping pain, *etc* I did not know then about the string sign, and our only roentgenologic evidence was that the fistula had communicated with the cecum

At operation, I developed this much thickened and enlarged cecum and determined upon its removal, probably with an anastomosis of the ileum to the transverse colon, but in removing the cecal portion, which was very adherent, I broke through an ulcerated area and into the intestine That left me with an infected field in which to work The lower ileum was somewhat thickened and enlarged but it was smooth and there was no external evidence of any ulceration or fistulous formation in that region The specimen when removed showed a very irregular, enlarged, and thickened cecum and a small portion of ileum

Rather than risk infecting the general peritoneal cavity by performing an ileotransverse colostomy, I was able to effect an end-to-end anastomosis, leaving an indefinite amount of somewhat thickened but dilated lower ileum The patient made a perfectly good recovery and was discharged the third week Subsequent roentgenograms show a normally functioning bowel

The patient, during the past four years, has been perfectly well and has gained 50 pounds in weight I think the result shows that I was justified in leaving a suspicious portion of the lower ileum, although I do not pretend to say that that is a correct procedure as a general rule I feel that, as Doctor Dixon says, the proper procedure is a complete resection in either one or two stages, when feasible

DR EDWIN P LEHMAN (University, Va) One of the most useful things that Ciohn did in his first communication on this subject was to divide the disease into four pathologic stages Interest, as far as the surgical treatment is concerned, has, of course, been largely directed to the later stages of the disease I have recently reviewed the literature in relation to the first or acute

phase There seems to be a good deal of difference of opinion as to whether or not the acute phase should be treated by radical operation

I am reporting (Review of Gastro-Enterology) a group of seven cases, seen at the onset of symptoms, all of them explored under the diagnosis of appendicitis, except one case that had had the appendix removed previously They were all treated with nothing more radical than appendectomy, which was performed not with the idea of curing the disease, but because the appendix was readily accessible Of these seven cases, two have been completely symptom-free for nine and one-half years One has been completely symptom-free for four years One has been symptom-free for a year, and in a recent check-up complete clinical and roentgenologic studies revealed no disease

It has seemed to me, on the basis of this experience, that the first attack is probably not the time to perform a radical operation Some of these cases will undoubtedly resolve It is a good deal safer at the first attack of symptoms, in the acute stage, to perform no surgery except that which is required for diagnosis, and possibly an appendectomy, so long as the latter is easy to do Radical surgery can follow, if simple exploration is not followed by resolution Such a course makes obligatory very careful observation of the patient after the exploratory operation

DR HARRY H KERR (Washington, D C) I would like to ask Doctor Dixon if they have had any recurrences, in their experience, in the large group of cases he reported I have recently had one that was quite illuminating, and Doctor Shearer of Washington has reported three recurrences with three resections in one case The patient is now well

The instance personally observed occurred in a woman who had lost some 60 pounds because of a long drawn out illness with diarrhea, vomiting, anorexia, *etc* An exploratory celiotomy revealed a regional ileitis, six inches in extent, two feet above the ileocecal valve, with the characteristic intestinal findings and tremendously enlarged nodes in the mesentery The involved bowel and thickened mesentery were resected, and an end-to-end anastomosis established She made an uneventful recovery and rapidly gained weight She remained apparently well for about a year, when she began complaining of a loss of appetite, with occasional crampy pains in the abdomen, a palpable mass could be felt in the lower right quadrant There had been left, I suppose, a foot and a half of ileum between the valve and the resection

We operated upon her again and found about six inches of the terminal ileum involved, with the usual characteristic, striking change between the diseased ileum and the perfectly normal cecum On eviscerating her pretty thoroughly, we found just below the site of the previous anastomosis a small area, perhaps two inches long, of definite thickening but without constriction, and in addition, perhaps a foot above the previous anastomosis, another area, two and a half or three inches long, with definite involvement

With the bowel well out on the table, it could then be seen that there was a difference in the appearance of the bowel between the segments of diseased ileum, and the flat, ribbon-like, perfectly normal ileum It was apparent that there was a difference between this normal ileum and the ileum between the actual areas of disease that could be appreciated only on comparison

A wide resection, from the perfectly normal, flat, thin, ribbon-like ileum, well above the disease to the transverse colon and an end-to-end anastomosis were performed I am interested to know if the bowel between the areas of frank disease was different from the normal bowel in which the second resection was performed

DR CHARLES G MIXTER (Boston, Mass) I would like to speak about one point in technic which I think might be of interest Lately, the question has arisen, on account of the number of recurrences that have been reported, of the possibility of this particular lesion being classified again as a medical lesion instead of a surgical one

Our experience has been that approximately 40 per cent of our cases have shown complications of fistulae, either to the large bowel, to the bladder or to the skin, or as multiple lesions Such lesions appear definitely surgical—surgery is used in other conditions where we do not necessarily expect to cure the underlying disease, for example, peptic ulcers If we can show that a good percentage of cases of regional enteritis which have been disabled, can be returned to health, it seems to me that the lesion should be classified as a surgical one

Recently, I looked up our cases during the past seven years, and the two oldest cases, seven years and six years after operation, have each put on about 50 pounds in weight, and they have returned to their occupations

I believe that possibly some of the recurrences that have been reported may have been due to inadequate removal of the mesentery If the mesentery is the original site of the disease, as perhaps Reichert's work would lead us to believe, or if, on the other hand, the lesion starts in the small bowel and then travels to the mesenteric nodes, in either case, there is a perfectly good probability of extension taking place to adjacent bowel after resection, if those infected nodes have not been or cannot be removed

I do not say that one can remove the complete segment of involved mesentery in all cases, but I do believe we should make the effort to make as wide a resection of the mesentery as we do of the bowel itself

DR JOHN HOMANS (Boston, Mass) Doctor Kern asked for information as to recurrences and among the six cases upon which I have operated There has been one recurrence, which was of so striking a nature that it is worth reporting, also, in some of the other cases, the limit of the disease has been so uncertain that I can hardly believe anyone could have been sure, without sectioning specimens from a long area of bowel, that he could tell how far the disease had spread

The recurrence was one of a typical ileitis in a man with a great many inflamed nodes in his mesentery, and a very considerable area of the mesentery was involved, so here I think that Doctor Mixter's suggestion as to the cause of the recurrence may apply

I resected an area including perhaps a foot above the disease, removed the cecum and the ascending colon, and made an end-to-side anastomosis The recurrence evidenced itself within two weeks The patient was then treated medically for a year or more, after which he was again explored So much disease was found in the mesentery and so much bowel apparently involved, that it was felt he was incurable A half-hearted attempt was made to carry him along by establishing an anastomosis between the normal bowel and the transverse colon, which did no good

He then went to Doctor Cohn, under whose direction he was subjected to a resection, since which operation, he has suffered another recurrence, so I fancy that he is actually incurable, perhaps for the reason that Doctor Mixter suggested—too much of his mesentery has become involved in the disease and causes reinfection of the bowel

I should also like to add that in two cases I have seen the disease in the cecum and ascending colon In one of these, I had resected around the corner of the transverse colon into what I thought was normal bowel, and

the pathologist reported that halfway across the transverse colon the disease was still present, so in that case nobody could have been sure.

Another recent instance occurred in a male, age 21, who had had the disease for exactly two hours, symptomatically, before I operated upon him. It was an unusual case, in which there was nothing to be noticed except a very slight thickening of the cecum and ascending colon and only slight dilatation of the lower ileum for perhaps a couple of feet. An appendectomy was performed. Subsequent roentgenologic examinations showed only the faintest possible involvement of the cecum. The rest of the bowel appeared completely normal.

I should add that there were a few large nodes in the mesentery, I feel that there was no way of telling how much should have been resected. My own feeling is that this disease is a rather moving one, that is, not by any means confined to the small bowel, that the extent of the disease in the mesentery sometimes makes it incurable, and that it may extend so far down the large bowel that no one, even on the operating table, can be sure of its extent.

DR CLAUDE F DIXON (closing) Just as frequently happens, the discussion of the paper has been more interesting than the presentation itself. Doctor Kerr has mentioned an important point, namely, that in this condition, which we have called regional enteritis, there may be apparently normal portions of bowel between involved segments. Five or six such cases have been observed at the clinic. In these instances, although there is no gross evidence of pathologic change in the intestinal wall, the apparently normal segment is markedly dilated, as a rule.

The early phase of segmental enteritis may produce rather marked symptoms without gross evidence of disease on the serosal surface of the intestine. A case upon which I operated serves to emphasize this point. The roentgenologist had made a diagnosis of terminal ileitis but I was unable to detect any gross abnormality in the ileum or cecum and I closed the abdominal incision without doing anything further than to make a careful inspection. Eight months later, because of an exacerbation of the symptoms, the patient was operated upon again. The surgeon found marked thickening of the wall of the terminal eight or ten inches of the ileum, and that this portion of the intestine was covered by a dense exudate. He resected the intestine and satisfactory convalescence followed. In these early cases, the ulceration in the mucosa is apparently the defect which the roentgenologist finds. By placing a light behind the suspected segment of intestine and transilluminating it, one may be able to detect a small defect such as an ulceration or a polyp. During the past few months I have employed a cold Cameron light for this purpose and have found it most helpful.

Doctor Lehman's case is extremely interesting to me. It emphasizes that even if a portion of the diseased bowel is left in situ, recovery may follow. However, I believe that when one is dealing with true segmental enteritis, extensive recurrence of the disease is most likely to follow unless radical resection is carried out. And I agree with Doctor Mixer that a radical excision of mesentery should be made if enlarged nodes are present.

Regarding the method of anastomosis of the intestine I realize that many surgeons employ end-to-end or end-to-side anastomoses, nevertheless, if I am to carry out the procedure I feel, as a rule, that the side-to-side method will be found the safest.

PERIANAL FISTULAE AS A COMPLICATION OF REGIONAL ILEITIS

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SINUS tracts and fistulae of various kinds constitute one of the most constant manifestations of ileitis, they originate in the distal ileum which then constitutes the proximal end of the tract. The fistulae terminate on a surface of the body, epidermal or endodermal. The most common site of termination is on the abdominal wall, the fistulous tract burrowing through the scar of a previous operation (usually an appendectomy). Where no operative scar is present on the abdominal wall, we have rarely seen fistulae. Other common sites of termination are segments of the colon, particularly the cecum, the ascending colon and the ubiquitous sigmoid loop of the pelvic colon, vagina, rectum or ureters.

Of late, in addition, we have received the oral description of a case of ileitis whose earliest and first manifestation was a fecal fistula, making its exit as a perinephric abscess in the right lumbar paravertebral area (Dr A Snapper of Amsterdam, Holland). Another case seen by one of us (B B C) presented four lumbar fistulae placed in linear arrangement vertically in the right lumbar area, accompanied by two inguinal fistulae, all of them discharging feces. In neither of these lumbar cases were intestinal symptoms noted, nor was there any suspicion of an intestinal disease until the fecal content of the fistulous abscesses became apparent.

One of the most common types of fistulae complicating ileitis, however, remains to be described, namely, the perianal fistulae. We were not at first conscious of the fact that anal and perianal fistulae constitute a frequent complication of the condition. But with more careful observation we have noted that eight out of 50 analyzed cases of regional ileitis exhibited anal fistulae as a complication, an incidence of 14 per cent. Probably this figure represents much too modest an estimate, for fistula-in-ano, unless questioned for in taking a clinical history, may easily be overlooked, and unless searched for in a complete physical examination, may be completely missed.

It is remarkable to note how frequently the fistula-in-ano was the first clinical manifestation of ileitis, even preceding consciousness of disturbed intestinal function. Such fistulae are usually local phenomena originating, presumably, in a crypt of Morgagni, infected by the contaminated ileal con-

tents transported to this spot, the tract makes its exit either in the anal region itself, commonly between or through external hemorrhoids, at the anocutaneous margin, on one of the buttocks, in the perineum, or, in women, as a rectovaginal fistula. They may be single or multiple, they may apparently close up for a time, but almost invariably reopen and leak a thin serous, purulent or fecopurulent discharge. They persist as long as the ileitis persists and is active, they close spontaneously when the affected small intestine is resected and may heal when a short-circuiting operation is successful. The rectovaginal fistula is the most persistent and requires surgical removal by dissection, a procedure which is often not successful and frequently must be repeated.

It is of course recognized that fistula-in-ano is a common disease associated with many diarrheal conditions of various origins. On the other hand, simple fistula-in-ano most frequently is a purely local manifestation, independent of any previous or associated disease, or accompanying simple constipation, the nonspecific fistula-in-ano is the type most commonly seen. Tuberculosis, while reputedly the cause of most of these fistulous tracts, is rarely found and is actually an infrequent offender, occurring in only about 1 per cent of instances of fistula-in-ano. Nonspecific ulcerative colitis is commonly complicated by perianal fistulae, according to Bargen, being present in 26 out of 697 instances, or 3.7 per cent of cases of ulcerative colitis. Probably any diarrhea, caused by inflammatory disease of the intestine, may be and is, complicated by fistula-in-ano, no matter how distant the source of the diseased segment. Submucosal infection in the crypts of Morgagni forms a low-grade abscess which breaks inward to the rectal mucosa and outward to the buttock or perianal region.

Noninfectious diarrheas do not produce perianal fistulae. We have never seen gastrogenous, neurogenic or allergic diarrhea, no matter how severe, complicated by fistula-in-ano.

The majority of perineal fistulae complicating ileitis are of local origin in the crypts of Morgagni. We have good reason, however, to suspect that there exist instances of *direct* fistulization from ileum to rectum or to perirectal spaces and then continuously downward to the perineum. The long fistulae originating from the terminal ileum are usually not direct in their course. They are very tortuous and conduct intestinal contents to the perineum. They become secondarily infected, particularly when they head downward and approach the pelvis. Low-grade pelvic abscesses frequently form, the infection seeps or spreads downward into the perirectal or ischiorectal spaces forming a perirectal abscess to the right of the rectal wall as it traverses the pelvis in its extraperitoneal course. This abscess continues to burrow downward and inward to point into the rectal cavity or somewhere near the anus. It is difficult to prove this point as we have not been able to follow such a fistulous tract throughout its continuity. But we have been able to trace, roentgenologically, the fistulous tract from ileum to pararectal abscess, again, in particular instances, we have been able to visualize an oc-

casional peri-anal external fistula, by injecting lipiodol or sodium iodide into its tract and, by roentgenography, prove that its course carries it upward and toward the ampulla of the rectum. Appended are three rather typical case histories which illustrate the existence and course of such "long" fistulous tracts.

CASE REPORTS

Case 1—We are indebted to Dr. Joseph Tomarkin of Cleveland, Ohio, and Dr. A. A. Berg for data on this case. Hosp. No. 399880, S. G., white, male, age 26, had been complaining of intermittent attacks of abdominal pain for one and one-half years. This pain localized in the center of the abdomen but was not associated with nausea or vomiting. Examination revealed tenderness over McBurney's point accompanied by definite spasticity of the right rectus abdominis. There was also tenderness in the right side of the pelvis on rectal examination. No masses were felt. Temperature was 100° F., leukocyte count, 16,400. Urine analysis was negative. *Preoperative Diagnosis*: Acute appendicitis.

Primary Operation—The appendix was found to be much enlarged and appeared gangrenous. It was situated in the mesenteric fold of the ileum and presented a small pocket of pus at its tip. The surgeon noted some redness and thickening of the ileum, contiguous to the appendix and extending for a distance of two and one-half to three inches along the terminal loop of the ileum. The appendix was removed and the abdomen was closed with drainage. The patient made an uneventful recovery. *Pathologic Diagnosis*: "Chronic catarrhal and subacute appendicitis and periappendicitis."

He was readmitted to the same hospital in Cleveland, Ohio, two and one-half months later, because of the recurrence of vague epigastric and umbilical pain. There had been no nausea or vomiting and his bowels were regular. Temperature, normal. On this occasion a mass was palpable by rectum, due to this a diagnosis of regional ileitis was suggested. Roentgenologic examination, however, showed no deformities in the ileum or cecum. As a result he was treated conservatively and when, after a few days, the mass, which had been felt by rectum, diminished in size, the patient was discharged.

One month later, he developed colicky pain in the left lower quadrant. There was no nausea or vomiting, diarrhea or constipation. He was running a subfebrile course and had lost a good deal of weight. Examination per rectum revealed a large mass. This was explored with a needle inserted through the lateral rectal wall, and pus was obtained. The abscess cavity was, therefore, drained through the rectum. Biopsy of some tissue from the wall of the abscess was reported as having an acute inflammatory reaction. After some improvement, the fever and pain recurred and the abscess cavity was again drained. About two ounces of pus were obtained and he began to improve rapidly. One month later, he was again readmitted to the same institution, suffering with marked diarrhea and a total loss of 75 pounds in weight. His stools were bloody and defecation was preceded by abdominal cramps. Roentgenologic examination of the small intestine, at this time, showed a typical ileitis with internal fistula formation. He was transfused and transferred to the Mount Sinai Hospital in New York City.

Secondary Operation—October 30, 1936. He was explored by Dr. A. A. Berg, and was subjected to an ileocecal resection with ileo-ascending colostomy and excision of fistulae between ileum and rectum. It was noted that the terminal foot of the ileum was thickened, indurated, and chronically inflamed. There were numerous peritoneal adhesions between loops of ileum. The mesentery of the affected ileum contained numerous large, oval, grayish nodes. A fistulous tract was present extending down along the right pelvic wall to the rectum about one inch above the anus.

Pathologic Examination, Gross. The resected intestine revealed chronic and acute

ulcerative terminal ileitis with multiple fistulae and subacute peritonitis. Eight centimeters from the ileocecal valve there was a perforation, about one centimeter in diameter, originating in the lumen of the ileum, and transversing the region of the mesentery. This was lined by reddish-gray granulation tissue. Four centimeters proximal to this fistula, and on the opposite side of the mesentery, there was another perforation of the bowel. The submucosa was thickened and showed numerous fistulous tracts. His postoperative course was complicated by a pneumonia which led to a lethal outcome after about two weeks.

Case 2—Service of Dr. Richard Lewisohn. Hosp. No. 384578. H. B., male, age 21, had developed pain, redness and swelling in the perianal region two years previously. An abscess was incised, pus evacuated and the area gradually, but not completely, closed over. About 19 months later a probe was inserted into the persistent opening for a variable distance upward. The fistula refused to heal and continued to discharge thin purulent material.

About six months before admission (one and one-half years after the first appearance of the fistula-in-ano) he developed cramp-like supra-umbilical pains, nonradiating and unrelated to meals. This pain continued for five weeks with afternoon rises of temperature to 101° F. Appendectomy was performed elsewhere and a "ruptured appendix with abscess" was found and drainage was instituted. The drain was removed in one week and the wound healed completely in 12 days. As he was about to be discharged, he developed pain in the right hip extending down to the thigh and associated with fever. The wound was reopened and again drained. A sinus to the abdominal wall formed which persisted for one month, but then closed, he was considered ready for discharge. At this time, he developed pain in the right lower quadrant where he noted a red, tender, painful, swollen area. This was incised and drained, and continued to drain up to the time he came under our observation, a period of four months. Six weeks before this period of observation the original incision reopened and remained as a draining sinus in the anterior abdominal wall. The tender mass in the right lower quadrant of the abdomen now reappeared.

Physical Examination—The following significant features were noted. There were two incisional scars in the right lower quadrant. The medial scar was a three inch pararectus incision beginning just below the level of the umbilicus. It presented a pinhead-sized opening at its lower end. This orifice was surrounded by granulation tissue and exuded pus on pressure. The lateral incision paralleled Poupart's ligament and extended just above it two inches from the anterior superior iliac spine. It was surrounded by granulation tissue and showed a greenish, foul discharge. There was a mass just lateral to the pararectus incision over which tenderness and rigidity could be elicited.

On the left buttock, one inch from the anus and in the "4 o'clock position," was a crusted polypoid mass from which pus exuded. This was surrounded by an area of induration above which a second opening could be seen.

Injection of lipiodol into the upper abdominal sinus, with occlusion of the lower one, outlined several tortuous sinus tracts. The greater part of the lipiodol traveled downward and puddled in the pelvis.

Gastro-intestinal roentgenograms showed no evidence of a lesion of the stomach or duodenum. Observations of the small intestine, made at hourly intervals, showed the jejunal loops displaced to the left by a mass in the right iliac fossa. The terminal ileum was narrowed, irregular and markedly deformed, indicating the presence of a nonspecific ulcerating lesion involving the ileum and cecum.

Operation—September, 1935. Dr. Leon Ginzburg. The ileum was cut across above the involved area, both ends were turned in and an ileotransverse colostomy was performed, thus excluding the mass from the fecal stream. His physical condition precluded any extensive exploration. His postoperative course was uneventful and the fistula-in-ano became asymptomatic. The discharge from the abdominal fistulae grad-

ually diminished, the fistula eventually closing. The fistula-in-ano closed spontaneously after the abdominal procedure, and has remained closed to date.

Case 3—Service of Dr. Richard Lewisohn, Hosp. No. 407492, S. F., white, female, age 24, had been perfectly well until six and one-half years before coming under observation, when she suddenly developed diarrhea while undergoing reducing procedure. There were as many as 20 nonbloody movements daily, accompanied by severe perineal pain. Fever was absent. Six months after the onset, a "rectal cyst" was observed in another institution and incised. Four months after this operation the diarrhea subsided spontaneously. A report from the above hospital indicated that she had had a perirectal and a vulvovaginal abscess, both of which had been incised and drained.

Six months after the first operation, she developed an abscess of the right labia majora, which was incised and drained. Shortly thereafter a swelling of the right buttock developed, which was also incised and drained, as was also an abscess of the left labia. The surgeon reported these as simple ischio-rectal abscesses. One and one-half years after the onset, and soon after the drainage of the second labial abscess, a rectovaginal fistula was found. This fistula was repeatedly operated upon, but never with successful issue. Feces were passed per vaginam and there was a persistent vaginal discharge. The failure of the rectovaginal fistula to close led to further investigation and it was found that there was a sinus tract in the rectovaginal septum which ran so far up that "it was necessary to leave the innermost portion of it behind because of the danger of entering the abdominal cavity." At this time a roentgenologic examination of the gastro-intestinal tract showed a stasis in the small intestine which was attributed to adhesions. Shortly thereafter, a celiotomy for "intestinal obstruction" was performed and an appendectomy was carried out. No details of the intra-abdominal findings were given.

About ten months before coming under our observation, she was suddenly seized with severe abdominal pain and admitted to another institution. Reports from this hospital indicate that the patient apparently had had a partial intestinal obstruction, which was attributed to a "chronic adhesive peritonitis." During all the years of her illness, the patient had suffered from diffuse lower abdominal cramps which were present daily, and were accompanied by frequent recurrences of her watery diarrhea. In the five weeks preceding our observations, the cramps and diarrhea had increased to the point of necessitating hospitalization.

Physical Examination—Mt. Sinai Hospital, New York. The patient was a well-developed and well-nourished young white female who presented a soft abdomen which was not distended or tender. There was a well-healed midline hypogastric scar. No intra-abdominal masses were felt. There were several well-healed scars in the perineum. Gynecologic examination showed a fistulous opening just within the vagina, about one-half inch above the fourchette, and leading into the rectum. Tuberculin tests were negative. Roentgenologic examination of the chest showed no abnormalities. Blood count showed only a mild secondary anemia. The blood Wassermann test was negative. Blood chemistry studies on admission were essentially normal. Examination of the stool showed the presence of occult blood but no ova or parasites. There were no serologic or cultural evidences of dysentery infection. Examination of gastric contents showed the presence of free acid. A gastro-intestinal series showed a dilatation of the distal jejunum and ileum, with evidence of an ulcerating lesion in the latter. Under observation, she progressively lost weight and had repeated episodes of fever and abdominal cramps.

Operation—A typical regional ileitis, with marked enlargement of the mesenteric nodes and massive adhesions which matted together various loops of small intestine was demonstrated. A fistula was found connecting the ileum and sigmoid colon. This was divided, and the involved ileum, cecum and ascending colon resected and an ileotransverse colostomy performed. It was then found that there was a fistulous tract in the

mesentery extending down toward the pelvis. It was not explored further due to the duration of the operative procedure.

Following a prolonged postoperative convalescence, the patient was discharged much improved, but with the rectovaginal fistula still patent. It was considered wise to postpone repair of this fistula to a later time.

Discussion—We may summarize these three cases as follows. In Case 1, a fistulous tract originated in the ileum and burrowed down into the pelvis, presenting itself as an abscess which reached to within an inch of the perineum before it was incised. The second case presented a small fecal fistula opening in the perineum. This was the result of an ischiorectal abscess which antedated the onset of the intestinal symptoms, but which eventually pointed to the presence of a regional ileitis. In addition, the patient presented two fistulae to the abdominal wall. The injection of lipiodol through the abdominal wall fistulae led to a cavity deep in the pelvis. A short-circuiting operation resulted in the spontaneous healing of all the fistulous tracts. In the third case, we were confronted with two fistulous tracts, both directed toward the pelvic floor—the one extending downward from the ileum to the ischiorectal fossa, the other extending upward from the perineum through the rectovaginal septum approaching the same area in the pararectal space.

In a recent analysis of the clinical histories of a series of 56 consecutive cases of regional ileitis, we were struck by the frequent occurrence of "fistula-in-ano" as narrated by the patient in discussing past gastro-intestinal disorders. Several of these patients presented perineal scars as evidence of previous surgical interference and in a few instances several nipple-like excrescences were found from which purulent material could be expressed. Objective data on such cases were observed in eight instances in this series, indicating an incidence of about 14 per cent.

Such perirectal or perianal suppuration would not be considered an unusual complication in a disease process so prone to manifest itself with diarrhea, were it not for its high incidence and unusual clinical features. In an analysis of 693 cases of chronic ulcerative colitis, Baigen found 26 cases of perirectal abscess and fistula-in-ano, which he considered to be due to infection of the crypts of Morgagni with subsequent invasion of the perirectal tissues and abscess formation. These figures would indicate an incidence of 3.7 per cent of fistula-in-ano or perirectal abscess in chronic ulcerative colitis. In a similar analysis of a mixed group of patients with various complaints referable to the anus, rectum or colon, he found fistula-in-ano to be present in 5 per cent of the total series.

The well-known tendency to intra-abdominal sinus and fistula formation shown by the pathologic process characteristic of regional ileitis, led us to believe that the perineal process might be another expression of the same burrowing capacity so frequently found in the production of fistulous connections between ileum and intra-abdominal viscera or abdominal wall.

These long or continuous fistulae are uncommon in comparison with the

more frequently observed simple, short fistula-in-ano. They are, however, exceedingly interesting and will bear careful clinical observation and recording. As a clinical manifestation, they frequently precede all symptoms which may cause suspicion of, or direct attention to the intestinal tract and particularly, the ileum.

For that matter, all fistulae which occur in association with ileitis may precede the consciousness of an intestinal disturbance. This applies to the fistulae in the abdominal wall which follow a futile exploratory operation, as well as to fistulae to segments of the colon, to the inguinal or lumbar regions, or fistula-in-ano. The original disease is of so subdued a nature and runs such a mild chronic course that the fistulae often precede the history or consciousness of diarrheal disturbances. In fact, of late we have seen ileitis with only constipation, but with fistulae-in-ano already recognizable.

Every case which presents itself with fistula-in-ano should deserve careful clinical preoperative study. The general conception that most fistulae-in-ano are tuberculous in origin is entirely erroneous, according to the pathologic records of the Mt. Sinai Hospital (Dr. Paul Klemperer), less than 1 per cent of granulation tissue removed at operation and subjected to study, reveals the tuberculous nature of such fistulous tracts.

Every case of fistula-in-ano is entitled to a proctoscopy, to rule out ulcerative colitis, to a careful roentgenologic study of the intestinal tract, to a roentgenogram of the chest to establish the existence or nonexistence of tuberculosis, and to a careful history and an even more careful physical examination.

In any case suspected of ileitis in which the roentgenologic findings are inconclusive and not convincing, the existence of one or more perianal fistulous tracts should materially support the diagnosis of an ileitis, providing of course that ulcerative proctitis or colitis is excluded.

Treatment—Perianal fistulae, para-rectal abscesses and rectovaginal fistulae originating from ileitis are best handled surgically by efforts directed to remove the primary disease. When the ileitis is entirely resected, the fistulae almost invariably close and heal permanently. Our experience with short-circuiting operations is insufficient, but we have reason to doubt that they will uniformly, or even in a majority of the cases, lead to healing of the fistulous tracts in the anal region, occasionally, however, such short-circuiting operations are successful in causing healing of the fistulae.

Persistent diarrhea is a deterrent to healing of such tracts, it is better to resect the ileitis in its continuity rather than leave a persistent focus of infection within the intestinal lumen with its recognized capabilities as a trouble-maker.

Where the fistulae fail to heal spontaneously after the ileitis has been properly handled, local excision of the tract, curettage and suture should be instituted, provided the bowel function has been restored to normal. In our experience the rectovaginal fistulae always require operation and cauterization, usually, unfortunately, with little success, so that many attempts are required before a satisfactory result can be obtained.

ACUTE CHOLECYSTITIS

THE RESULTS OF OPERATION WITHIN FORTY-EIGHT HOURS OF THE
ONSET OF SYMPTOMS

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THERE has been a steadily increasing interest in early operation for acute cholecystitis during the past decade, but the term "early operation" seems to mean anything from early in the disease to soon after admission to the hospital, although the patient may have been previously ill at home for some days. To evaluate results, it is desirable to set a definite time and, for the purpose of this study, we have chosen the first 48 hours from the *onset* of the symptoms of the acute attack.

TABLE I

OPERATIONS FOR ACUTE CHOLECYSTITIS WITHIN 48 HOURS OF THE ONSET

Surgeon	Number	Cholecystectomy	Cholecystostomy	Deaths
Graham ¹	20	18	2	1
Heuer ²	50	49	1	2
Stone ³	2	2	0	0
Walters ⁴	7	6	1	0
Taylor ⁵	19	?	?	1
Graham and Hoefle	51	51	0	2
Kunath ⁶	6	0	6	0
Zinninger ⁷	12	?	?	0
Totals	167	126	10	6
Mortality Percentage				3.59%

Table I shows that in 167 cases which were operated upon within 48 hours of the onset, there occurred six deaths, a mortality rate of 3.59 per cent. We are more concerned with the *promptness* of the operation than with the *type* of procedure, but cholecystectomy was the operation of choice in these cases, while cholecystostomy was reserved for the more critical cases.

There are certain factors that make a cholecystectomy for acute cholecystitis more difficult than one performed in the quiescent period. The gallbladder is often tense and distended. The tissues are more friable and the bleeding is more profuse. There is more swelling around the cystic duct. It may be necessary to aspirate the gallbladder, and we usually prefer in these acute cases to remove it from above downward, controlling the bleeding from the liver bed by the pressure of a gauze pad and a retractor. The cystic duct is carefully ligated, using traction toward the common duct instead of away from it. This prevents the possibility of pulling the cystic duct off accidentally at a lower level than was intended. It, for any reason, the cystic artery escapes and bleeds, it is easy to control this and secure a

dry field by the use of a small angular retractor or the finger in the foramen of Winslow making pressure on the hepatic artery until the bleeding vessel has been clamped and ligated. An oozing liver bed, that cannot be obliterated, can be quickly peritonealized and rendered dry by a free omental graft lightly tacked in place by a few interrupted sutures. A large percentage of cultures taken during the first 48 hours remain sterile and, therefore, infection is not a major problem at this time.

It has frequently been said that acute cholecystitis is not like acute appendicitis, and that there is not the same necessity for prompt operative interference. The statistics in Table II show the mortality at various periods after the onset of symptoms.

TABLE II
ONE HUNDRED CONSECUTIVE CHOLECYSTECTOMIES FOR ACUTE CHOLECYSTITIS
From the First Surgical Service of the Methodist Hospital, Brooklyn, N. Y.
January 1, 1929, to October 1, 1937

Onset of Symptoms to Operation	Edematous		Suppurative		Gangrenous		Perforated	
	No.	Died	No.	Died	No.	Died	No.	Died
Up to 48 hours*	26	0	19	0	3	0	3	2
2 to 5 days†	14	1	8	1	5	0	0	0
5 days or more‡	14	1	3	1	4	2	1	1
	—	—	—	—	—	—	—	—
Total	54	2	30	2	12	2	4	3

* Acute cholecystitis operated upon within 48 hours—51 cases—2 deaths—3.92 per cent.

† Acute cholecystitis operated upon 2 to 5 days—27 cases—2 deaths—7.40 per cent.

‡ Acute cholecystitis operated upon 5 days or more—22 cases—5 deaths—22.72 per cent.

Total mortality in 100 cases—9 deaths—9.0 per cent.

A delay of more than five days gives a high operative mortality, and raises the question of whether operation should be performed or delay advised. This must be decided for each individual case. When operation is performed in these cases, the further question of what operation is indicated will arise. Note that there were three patients with gangrenous gallbladders, and there were also three patients with perforated gallbladders, within 48 hours of the onset of the attack, and two of the latter died. Harvey Stone³ cites an instance of a totally gangrenous gallbladder, with autolysis, which he found at operation, seven hours after the first severe pain which marked the onset. Gangrene was also present in another case. In a third patient, who was being studied for obscure digestive symptoms of three months' duration, a perforation of the gallbladder with resultant peritonitis suddenly occurred, necessitating an emergency operation. In Kunath's⁶ six cases, there was one patient with a gallbladder already gangrenous, and two cases in which perforation had occurred. In Taylor's⁵ 19 cases, operated upon within 48 hours, five were already gangrenous. These are not rare or unusual events. Most of the recently published series of cases of acute cholecystitis show an incidence of gangrene of about 20 per cent.

In the last analysis, the greatest emphasis must be placed upon the mor-

tality statistics. Whatever method will save the most lives should be employed. In Pennoyer's⁸ series of 300 cases of acute cholecystitis, treated in the Roosevelt Hospital, where the general policy was to delay whenever possible, the mortality was 10 per cent. This presents a striking contrast to the 3.59 per cent mortality in the cases operated upon within 48 hours of the onset, and is a strong argument in favor of a determined effort to obtain these cases for operation within 48 hours. Consideration must also be given to the other disadvantages of delay, namely, the days of pain, the sleepless nights, the starvation and debility, the long hospitalization and increased expense.

It is difficult to see two sides to this question, when it is so evident that a lowering in mortality could be accomplished so easily by education of the laity and cooperation between the family physician and the surgeon to secure a prompt operation, early in the attack, for every person suffering from acute cholecystitis who is a proper operative risk.

SUMMARY

(1) A series of 167 cases of acute cholecystitis operated upon within 48 hours of the onset of the attack has been collected. The mortality was 3.59 per cent.

(2) The difficulties of operation in the acute stage have been discussed, and also the methods that can be employed to minimize these dangers.

(3) An earnest plea is made for education and effort to secure operation in acute cholecystitis within the first day or two of an attack.

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EPIDERMOID CYSTS OF THE SPLEEN

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EPIDERMOID cysts of the spleen are apparently very rare. In a fairly careful search of the literature we have been unable to find any cases of this condition reported since 1933, when Shawan¹ collected three cases and added one of his own. Custer,² in 1937, stated that he had seen five cases of simple epidermoid cysts of the spleen in 5,000 autopsies, but no description of them has been found in the literature. Shawan cites Libarsch as having recalled a case but no report was made. The great rarity of this pathologic condition probably accounts for the fact that epidermoid cysts are not mentioned in most surgical text-books and are omitted from some classifications of cysts of the spleen.

We were entirely unfamiliar with this peculiar tumor formation until our attention was attracted to it by the appended case.

Case 1—Female, age 7, had been in good health until February, 1937, when she developed an upper respiratory infection. The family physician in his routine examination discovered a tumor in the upper left quadrant of the abdomen which he thought was associated with the spleen. He prescribed roentgenotherapy, but as the tumor remained unchanged after eight weeks' treatment the child was sent to the Children's Memorial Hospital. At the time of her admission, June 21, 1937, the child had no complaints and appeared to be in good health. Her past history was essentially negative.

Physical Examination disclosed nothing abnormal except a mass in the left upper quadrant of the abdomen in the region of the spleen. The tumor appeared to be freely movable and extended at least two inches below the costal border and more mesial than the usual splenic border. It extended upward nearly to the nipple, making the lower edge of the thorax bulge slightly on that side, and during inspiration the mass could be seen moving downward in the abdomen. As the tumor emerged from under the costal margin a sharp line running parallel to the costal border was palpable and the fingers sank in above the mass. Pulse, respiration and temperature were normal, as well as her blood count and uranalysis. The Wassermann test was negative but the Mantoux skin test was strongly positive.

A fluoroscopic examination of the colon showed that the splenic flexure was depressed downward with a constant position beneath the mass but with no evidence of adhesions or obstruction. A diagnosis of a splenic tumor, due to either tuberculosis or a neoplasm, was made.

Operation—Under ether anesthesia, the abdomen was opened through an upper left rectus incision. A large cystic mass, intimately attached to the spleen, presented immediately. The cyst was tapped and 520 cc of chocolate-colored, turbid fluid aspirated. Removal of the spleen with the cyst was then easily accomplished.

Pathologic Examination—*Gross* The specimen is an almost globular, cystic mass,

with a rim of splenic tissue at its equator. Its longest diameter is 15 cm, its widest 12 cm. The splenic tissue at the hilus is replaced by a cystic dome (Fig 1a), measuring 12x8x3.8 cm. There is a patch of gray-white tissue (Fig 1b), moderately firm in consistency, 4.5x3.0x0.4 cm, slightly lateral to the peak of this dome. There is a similar

FIG 1

FIG 2



FIG 1—Exterior of the specimen (a) Cystic dome at hilus region (b) Fibrous patch (c) Fibrous patch (d) Costal portions of cyst (e) Triangular projections of splenic tissue

FIG 2—Internal surface of the specimen (a) Irregularly disposed trabeculae (b) Crypts bounded by the trabeculae (c) Cyst capsule (d) Surfaces made by cutting the splenic tissue

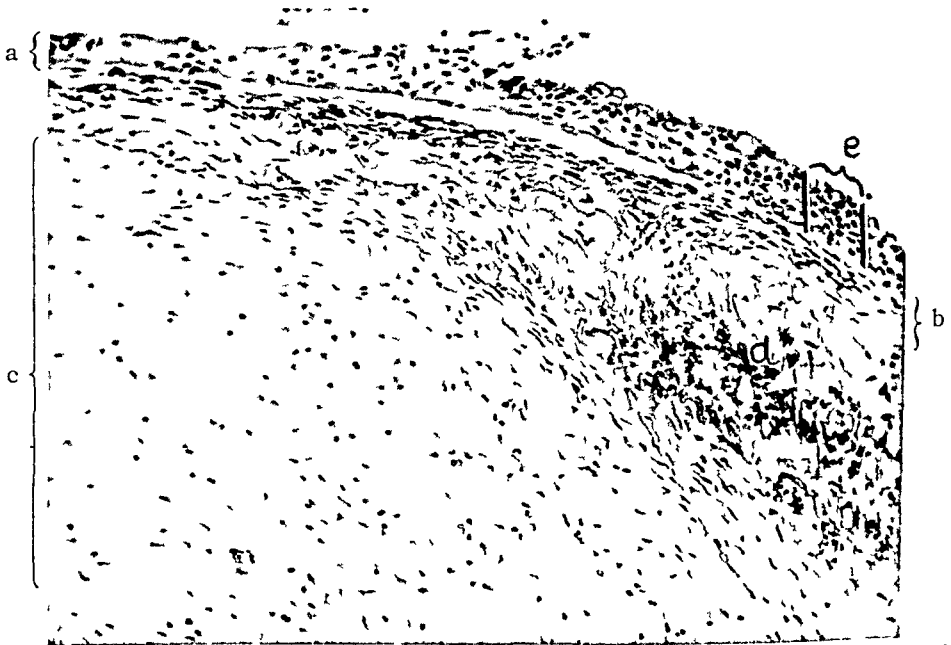


FIG 3—Inner wall of the cyst (H & E X100) (a) Stratified epithelium (b) Subepithelial fibrous layer (c) Collagenous cyst capsule (d) Hemorrhagic area within the collagenous tissue (e) Low power view of Fig. 4

patch (Fig 1c) 2x2.5 cm at the junction of the hilus to the body of the spleen. The costal portion (Fig 1d) of the specimen is cystic, bulging and covered by a thin, gray-white tissue, measuring 7.5x4.5x0.05 to 0.1 cm.



FIG 4—Epithelium of the cyst (H & E $\times 1100$) at Fig 3e (a) Epithelial cell with surrounding canaliculi and intercellular bridges

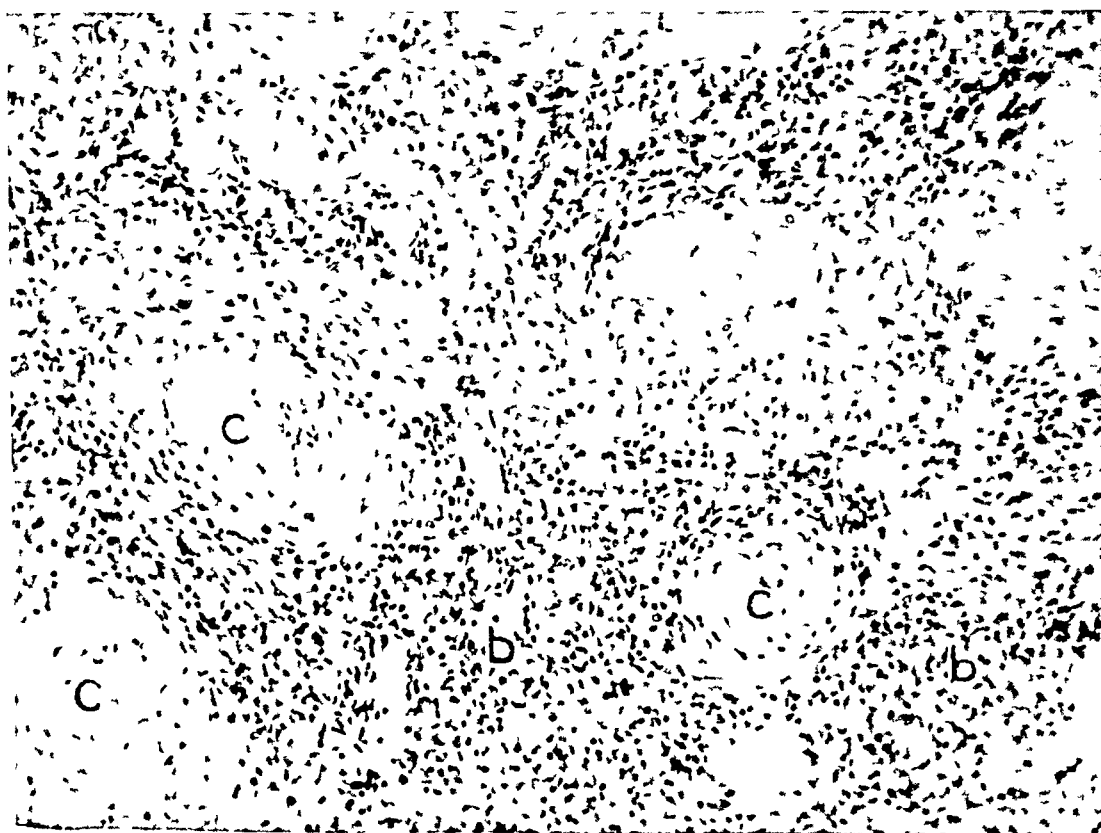


FIG 5—Boundary of cyst capsule and splenic tissue (V H & E $\times 100$) (a) Innermost portion of collagenous cyst capsule (b) Sparse splenic elements (c) Heavy fibrous trabeculae replacing the parenchyma

Internally there is but one large cyst present, its content 520 cc of sterile, chocolate-colored fluid somewhat thicker than blood serum in consistency. The internal surface of the cyst contains a large number of irregularly disposed trabeculae (Fig 2a) measuring from less than 1 to 8 Mm in thickness, bounding shallow crypts (Fig 2b). The trabeculae are gray-white to brown-gray. Upon this internal surface there is plastered an adherent, wavy, brown deposit. The cyst capsule (Fig 2c) is made up principally of gray-white fibrous tissue 2 to 4 Mm in thickness, except at the costal portion previously mentioned.



FIG 6—(H & E $\times 100$) (a) Basal layer of the stratified epithelium (b) Stratified epithelium beyond the basal layer (c) Fibrous tissue with an infiltration of plasma cells, monocytes as well as red blood cells

The cyst completely displaces all the splenic tissue except that bordering on the hilus region, where a rim of this tissue persists, the largest area a triangular projection (Fig 1c) 4.3 \times 2.3 cm. The remainder of the splenic tissue forms a thin layer over the central portion of the cyst capsule, diminishing in thickness peripherally, almost in proportion to the distance from the hilus.

Surfaces made by cutting the splenic tissue are bluish-purple (Fig 2d), the markings are not unusual except for an increase in gray-white fibrous elements adjacent to the cyst capsule.

Histology—The cyst epithelium, where present, varies from one to nine cells in thickness, is stratified, with no keratinized cells on the surface. In the thinnest portions there is present a single or double row of flattened cells. The nuclei of the cells in the stratified epithelium are basophilic, irregularly round, oval to flat with a tendency of the long surfaces of the nuclei to lie parallel to the epithelial surface. The cytoplasm is palely basophilic and consists of irregular platelets separated from each other by an intercommunicating network of slender canaliculi. Throughout the lumina of the canaliculi there are fine linear "bridges" in nearly parallel rows, roughly perpendicular to the walls of the canaliculi (Fig 4)

Figure 6 shows underlying the epithelium a layer of fibrous tissue, two to five cells thick, closely packed, the cells parallel to the epithelial surface. Separating the epithelium and underlying fibrous tissue layer from the splenic tissue is a thick layer of irregular trabeculae of the underlying spleen. There are small hemorrhages in each layer described, recent in nature (Fig 3d)

The splenic tissue is not altered except for fibrous replacement of the parenchyma in almost a direct proportion to the contiguity with the collagenous tissue (Fig 5)

Large areas of the cyst, as that of the costal portion, consist of nothing but fibrous tissue, no epithelial or splenic elements being present. No hair follicles, sweat glands, pigment layer or other skin appendages are present.

In the gummy, brown deposit adherent to the epithelium there are present many macrophage cells with much vacuolization. There is also present a relatively small number of red blood cells.

Studies of the fluid removed from the cyst

Bacteriology—Direct smear showed cell debris but no organisms.

There was no growth on various culture medias.

Chemistry—N P N—28.6 mg

Total protein—5.4

Cholesterol—Sludge, 1st spec—620 mg, 2nd spec—780 mg, fluid, 1st spec—168 mg, 2nd spec—178 mg

Our attention was further drawn to the subject by a case which was studied by Dr H Gideon Wells, pathologist at the University of Chicago, and which we are permitted to report through the courtesy of the attending surgeon, Dr W L Jeffries.

Case 2—Male age 6 months, was born of apparently normal parents August 28, 1935. Both parents showed a negative Kahn test. On February 22, 1936, he was brought to the hospital because of fever and fretfulness. He had had recurrent attacks of vomiting and abdominal distress for a week previous to admission.

Physical Examination was negative except for the presence of a large round mass in the left hypochondrium and lumbar regions. A fluoroscopic examination of the gastrointestinal tract showed that the stomach and intestines were displaced to the right by a tumor the size of a grapefruit, which occupied the left hypochondrium. Roentgenologic examination of the urinary tract, after the injection of diodrast, showed a very tortuous, dilated left ureter and a marked dilatation of the left kidney pelvis with a large shadow in the left upper quadrant suggestive of a hydronephrosis. An examination of the blood showed nothing abnormal. A diagnosis of hydronephrosis was made.

Operation—February 24, 1937. Under ether anesthesia, what was thought to be the left kidney was drained through a retroperitoneal approach. A quantity of clear, watery fluid with an acid reaction was removed. Unfortunately the fluid was not analyzed further. The child was discharged with a draining sinus March 4, 1936.

About six weeks later the patient was readmitted, because the sinus continued to drain, and on April 17, 1936, the left kidney and spleen were removed. The child expired the following day.

Pathologic Examination—Gross Figure 7 shows the fixed specimen which weighed 23 gm (19 gm normal for seven and one-half months). The capsule is smooth except for a small area at the lower pole where it is lacking. There is present an intrasplenic cystic cavity 4x2x1 cm centering about the hilus. Internally, there are present trabeculae similar to those seen in Case 1, except that they are brown-gray, fewer and broader, and the crypts fewer, deeper and broader. The cyst is surrounded by a heavy fibrous capsule 2 to 3 Mm thick, containing focal areas of calcification, and is covered throughout by splenic tissue except at the hilus. The impression gained by examination of the spleen was that originally there was present an extrasplenic cyst attached to the intrasplenic portion. No further description is given.



FIG 7—Case 2 Cut surfaces of the spleen showing interior of epidermoid cyst

The cyst fluid, described at the first operation, was clear, watery and acid in reaction.

Histology—The cyst epithelium is stratified. There is present a basal layer of dark staining cells two to five rows in thickness. These cells contain oval, basophilic, vesicular nuclei with the longest surfaces perpendicular of the epithelial surface. The cytoplasm is palely basophilic and consists of irregular platelets separated from one another by canaliculi and "bridges" similar to those present in Case 1. The epithelium beyond the basal layer contains as many as 20 or more cells in various stages of degeneration with fragmented and pyknotic nuclei and with cytoplasm made up of little else than a palely eosinophilic cellular membrane. This epithelium has thus the appearance of a fine eosinophilic network with pyknotic nuclei in the apertures of the net. There are no keratinized cells present.

Underlying the basal layer of the epithelium there is present a thick layer of fibrous

tissue, in some areas moderately loose, in others moderately compact Within this layer is present an infiltration of monocytes This fibrous tissue is continuous with the fibrous trabeculae of the spleen Many small, scattered hemorrhages are present in the fibrous layer

The splenic tissue is not altered except for fibrous replacement of the parenchyma adjacent to the fibrous layer No hair follicles, sweat glands, pigment layer or other skin appendages are present

DISCUSSION —Epidermoid cysts of the spleen are usually large, solitary, and lined with stratified pavement epithelium with prominent intercellular bridges No other epidermal or dermal elements have been found in the cases reported, but Custer has stated that some have been described in which the cavity was filled with sebaceous material and hair These cysts have been reported to have weighed as much as 3 Kg and to have contained up to 1,500 cc of watery, chocolate colored fluid usually containing cholesterol

The general structure of these cysts is strikingly similar from the trabeculated inner surface to the fibrous capsule and secondarily compressed spleen The splenic tissue is usually unaltered except for gross compression and fibrous replacement adjacent to the cyst capsule

All clinical symptoms associated with these tumors may be explained on the basis of compression of the surrounding viscera or abdominal distress from the dragging weight of the splenic mass

Because the clinical picture is not distinctive the diagnosis is usually obscure Pressure on the left kidney and ureter may produce confusing roentgenographic findings suggestive of urinary tract obstruction as in Case 2

Roentgenologic examination of the gastro-intestinal tract will usually demonstrate a downward displacement of the splenic flexure of the colon Attention was called to this finding by Ostra and Makaree This was present in Case 1 but it is merely considered indicative of a splenic tumor In all probability epidermoid cysts, because of their rarity and nondistinctive clinical findings, will be diagnosed only after a histologic examination

The treatment employed in all cases has been splenectomy When the abdomen is open, aspiration of the fluid content of the cyst, as suggested by Shawan and employed by us in Case 1, greatly facilitates the removal of the spleen with the attached cyst However, it is very necessary to be sure that the cyst is not parasitic before employing this procedure because of the danger of peritoneal contamination

No satisfactory explanation of the origin of epidermoid cysts of the spleen has been offered A problem arises with the assumption that epidermoid epithelium is necessarily ectodermal in origin, and from such an assumption the necessity of accounting for ectoderm in an organ presumably arising from the mesenchyme

An origin by *ectodermal metaplasia* similar to that of dermoid cysts has been suggested by Pohle³ This idea is supported by Custer's discussion, as well

Santy, quoted by Shawan, suggests the possibility of *displacement of the wolffian body*, as does Dinand⁴ The wolffian body may produce transitional

epithelium which under certain circumstances, such as a vitamin A deficiency, may become stratified and squamous

Shawan discusses *autochthonous formation*, according to which theory the mesoderm is capable of producing the products of any of the other primary germinal layers, including stratified squamous epithelium

Schneider⁵ was of the opinion that during splenic development some of the coelomic cavity content capable of forming epidermis was enclosed in the spleen. According to the studies of Thiel and Downey,⁶ the coelomic mesothelium definitely contributes to the development of the mammalian spleen

SUMMARY—Herein are reported two instances of epidermoid cyst of the spleen, occurring in a girl, age 7, and a boy, age 6 months. All the patients previously reported were in the second decade of life. Case 1 meets in every respect the criteria of diagnosis. Case 2 has a few questionable features, namely, that the removal of the spleen took place two months after drainage with epithelialization from without as a possible result, that there is evidence of infection of the wall of the cyst with its possible effect on epithelial type, and that the fluid removed surgically was found to be clear rather than chocolate colored. However, Case 1 probably represents a true example of an epidermoid cyst of the spleen.

This paper is presented as a contribution to the very limited knowledge of this rather rare and interesting pathologic condition, with the hope that it may stimulate the report of additional cases and thus perhaps verify Custer's idea that epidermoid cysts of the spleen are possibly not as rare as has been supposed.

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EMBRYOMA OF THE KIDNEY (WILMS' TUMOR)

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EMBRYOMA of the kidney is one of the most malignant growths of early life and it has a very high mortality. Some divergence of opinion has developed in recent years as to the most desirable plan of treatment for this condition. In many clinics preoperative irradiation, nephrectomy, and postoperative roentgenotherapy are employed as the therapeutic plan of choice. In others, nephrectomy is advocated as soon as the diagnosis is made. Some surgeons advocate a posterolumbar incision, while others see the advantage of a transperitoneal approach.

The present communication attempts to evaluate the facts available from a partial review of the literature, and in addition the study of 58 cases occurring in the Surgical Service of the Children's Hospital of Boston. Some of these cases were previously reported, in 1932, by my former associate, Dr Charles G. Mixer.¹ Of these 58 cases, 13 have been discarded for one of two reasons—either the patient was lost track of after operation or a pathologic specimen was not obtained by operation or autopsy. Of the remaining 45 patients, 44 were operated upon and one died without operation, but a postmortem examination was made. Therefore, in every instance a pathologic as well as a clinical diagnosis is at hand, and in every case the result of the treatment is known.

It is unnecessary to review the theories of pathogenesis, as that has been ably done by others, and the facts still remain a matter of surmise. It is imperative, however, to define these tumors from a pathologic and microscopic point of view, as the nomenclature is still confused, even in recent articles. Dr Sidney Farber has kindly contributed these data.

Pathology—The embryoma of the kidney is a large, solid, grayish-white, encapsulated, malignant tumor probably of congenital origin. It is surrounded by a dense connective tissue capsule which is continuous with that of the kidney. The kidney usually merges gradually with the convexity of the tumor, and is separated from it by a layer of connective tissue of microscopic to gross proportions. In general, the tumor cannot be freed from the kidney. Nodules are sometimes found within the substance of the remainder of the kidney. When rapid growth occurs, hemorrhage and softening in parts of the tumor are found.

Sometimes definite, scattered cysts may be encountered. The capsule is usually tense and occasionally the tumor bulges in irregular masses at one or more places on the external surface. The pelvis of the kidney may be com-

pressed, normal, or, rarely, dilated. Pressure atrophy is usually present in the remainder of the kidney.

On microscopic examination the tumor presents a varied appearance. All stages from undifferentiated to partially differentiated cells of epithelial origin and of the connective tissue series (smooth muscle, striated muscle,



FIG 1—Photomicrograph of section of embryoma of kidney (S 37 483). Note tubular arrangement of epithelial cells. The midportion consists of tumor cells of the fibroblastic series (Hematoxylin and eosin, $\times 100$).

sometimes bone and cartilage) may be found in the same tumor (Figs 1 and 2). In some instances one type of cell may predominate. It is not possible to predict, with accuracy, the nature of the type of cell from the gross appearance of the tumor. Various degrees of activity are demonstrable in the same

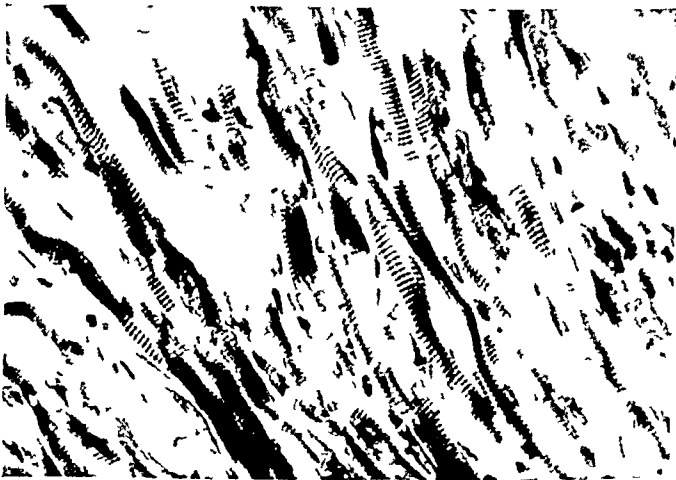


FIG 2—Photomicrograph of section of embryoma of kidney (S 37 483). This portion of the tumor consists entirely of striated muscle fibers (Phosphotungstic acid hematin stain, $\times 500$).

tumor. Extension into small branches of the renal vein or into the renal vein itself, or invasion of the pelvis of the kidney may be encountered. The tumor is characterized by (1) Variegated histology, (2) rapid growth after a period of slower activity, (3) the common occurrence of hemorrhage and necrosis

EMBRYOMA OF THE KIDNEY

which may lead to rupture of the capsule, (4) the possibility of invasion of the renal vein or the pelvis of the kidney, (5) a tendency to reach a large size before metastases occur, (6) the frequency of local recurrence and metastasis to the regional lymph nodes or remote metastasis through the blood stream to the lungs

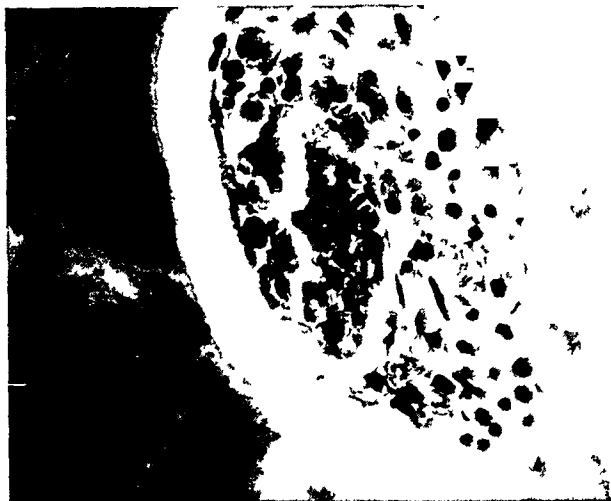


FIG 3—Photomicrograph of section of embryoma of kidney (S 38 40) Note well developed bone marrow surrounded by dense bone, found in one portion of the section (Hematoxylin and eosin, $\times 500$)

It should be emphasized that these solid tumors of the kidney in childhood should be grouped under the term embryoma of the kidney (mixed tumor of the kidney, Wilms' tumor) despite the varied gross and histologic features which may be encountered. All tumors of this type are highly malignant

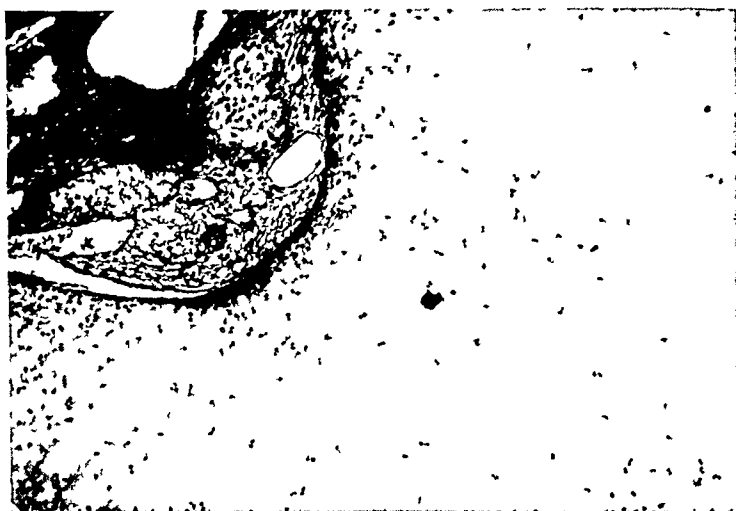


FIG 4—Photomicrograph of section of embryoma of kidney (S 37 483) Note well developed cartilage. In upper left hand corner is an area of loose connective tissue surrounding small islands of cartilage. The remainder of the tumor in this section consists of striated muscle and epithelial elements (Aniline blue stain, $\times 100$)

The finer classification of the tumors in this group according to histologic structure is for the present, at least, of interest only to the pathologist, but has no important bearing on the prognosis or the treatment. Of real im-

portance in the pathologic examination of surgically removed embryomata of the kidney are factors, such as degree and extent of hemorrhage and necrosis, rupture of the capsule, invasion by the tumor of the renal veins or the pelvis of the kidney, and extension of the tumor through the capsule

In infancy and childhood embryomata of the kidney must be differentiated from several other solid tumors which occur in the kidney region. The sympathetic neuroblastoma, which arises from the medulla of the adrenal gland or from medullary tissue in the immediate vicinity of the adrenal gland, is usually reddish-purple in color, well encapsulated, and is often firm and nodular in consistency. The kidney below the tumor is usually intact, although true invasion of the kidney may be found. Metastasis to the skeleton, liver or orbit takes place usually before the neuroblastoma reaches the size of the average embryoma of the kidney. The neuroblastoma on microscopic examination may contain cells of the sympathetic series in various stages of development (sympathogonia, sympathoblasts, or neuroblasts). In well fixed, suitable material the cells of the neuroblastoma are large, cylindrical and pyriform, and are often arranged in pseudorosette formation around a central zone, containing delicate fibrils representative of axis cylinder processes. Hemorrhage, often massive in type, and necrosis are common findings. Direct extension to neighboring viscera may take place before distant metastasis occurs.

The hypernephroma of the kidney, or the Grawitz tumor, is a solid tumor which arises within the kidney. We have not encountered a single example of hypernephroma in the last 20 years at the Children's Hospital. From a study of the literature, it appears likely that a true hypernephroma is of very rare occurrence in infancy and childhood, and that the term hypernephroma has been used loosely to designate an embryoma of the kidney in many instances. It is important to differentiate sharply between these two totally different tumors of the kidney. The hypernephroma is usually yellow in color in contrast to the grayish-white appearance of the embryoma of the kidney. The microscopic appearance is highly characteristic. The cells are large and have a clear to foamy cytoplasm. They grow at times in alveolar or tubular arrangement or in cords or nests of cells arranged in a fashion resembling somewhat the structure of the adrenal cortex.

Another tumor in the kidney region is the massive "unattached" retroperitoneal embryoma of renal anlage origin. This may be found on either the right or left side, or may grow nearer the midline. The tumor on gross and microscopic examination resembles closely the embryoma of the kidney. It is not attached to the kidney.

Diagnosis—The age incidence of embryoma of the kidney is of considerable help in arriving at a diagnosis of this condition. In our series the average age was two years and three months, which corresponds moderately closely to other series found in the literature. Our youngest patient was two months and the oldest child was seven years old.

In this group there were 26 females and 19 males, while in other series a slight predominance was found among the males

The occurrence of the tumor was equally divided between the two sides 22 occurred in the left kidney and 22 occurred in the right kidney, while in one patient the growth was bilateral

Therefore, it is apparent that statistics are of little diagnostic value except to show that this type of tumor is common in the first three years of life when other kidney tumors are rare, while in later life the reverse is the rule

The diagnosis of renal embryoma is not usually very difficult The main factors in arriving at the correct diagnosis are the clinical history and the palpation of the abdomen Embryonal kidney tumors seldom give symptoms other than those of enlargement of the abdomen, and sometimes symptoms from pressure on the adjacent organs The parent brings the child to the hospital, or to the physician, because she has noticed the child's abdomen increasing in size Unfortunately, it is very common for these infants to remain in an apparently excellent state of general health and without complaints, even after the tumor has assumed enormous proportions The child's apparent good health often results in delay before medical advice is sought This delay adds to the high mortality

On abdominal palpation these tumors feel solid, are not tender or fluctuant, and their location in the kidney region can be determined by bimanual examination—one hand in the costovertebral angle and the other on the front of the abdomen The anterior hand may often outline the tumor as extending to the midline or beyond and well down into the iliac fossa Occasionally, the tumor feels nodular but more often it is smooth and rounded It is usually not mobile

The urinary findings are seldom helpful in making a diagnosis Occasionally, one finds a few red or white cells, but more often the urine examination is negative and the N P N is within normal limits

Pyelograms, either intravenous or retrograde, may be suggestive but cannot be considered conclusive evidence of the presence or absence of embryoma of the kidney A distorted pelvis may be present in other conditions and an absolutely normal appearing pyelogram may exist in the presence of a very large embryoma (Fig 10A and B, and Fig 9) Though it has been our practice to obtain an intravenous or retrograde pyelogram in all cases where the diagnosis is in doubt, there are certain valid objections to making the latter a routine practice

In the age group in which this tumor occurs, the cystoscopic examination requires a general anesthetic, which means a delay before the nephrectomy Furthermore, it is only in the exceptional instance that the separate urine from each kidney has diagnostic significance The one strong argument in favor of routine cystoscopic examination is the desirability of knowing the renal function of the unaffected kidney

Aspiration biopsy, as recommended by some writers, has proved unreliable in our hands as a diagnostic method, unsafe as a surgical procedure, and is

quite likely to cause implantation recurrence. We abandoned the procedure almost 20 years ago. It seems, at least, theoretically important that as little trauma should be occasioned in handling these patients as is consistent with making a probable diagnosis. We know that the malignant cells may be cast off into the blood stream at any time and feel even slight trauma may facili-



FIG 5(A)—Photomicrograph of a section of kidney, the seat of an embryo (S 36 370). Note the small cluster of tumor cells in branch of renal vein (arrow). Note compressed renal tissue above the vein. (Hematoxylin and eosin, $\times 130$)

tate this incident (Fig 5A and B). Our convictions are strong enough along this line to not allow these patients to be examined by a multitude of students or in fact by any more people than is absolutely necessary.

Although numerous pathologic conditions might have to be differentiated

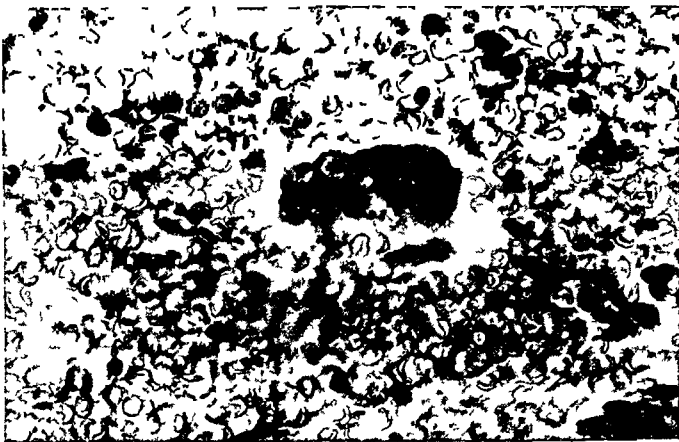


FIG 5(B)—Photomicrograph of portion of field shown in (A) (arrow). Note cluster of tumor cells surrounded by erythrocytes in renal vein. (Hematoxylin and eosin, $\times 900$)

from embryoma in the diagnosis, there are only two which have caused us much concern in the age group in which this disease occurs. These two are retroperitoneal neuroblastoma and hydro- or pyelonephrosis. The neuroblastomata are not so very rare, in our experience, and resemble the embryoma in being rapidly growing, and often distort the renal pelvis. The points of

dissimilarity are that the neuroblastomata are commonly nodular, extend earlier to both sides of the spine, and do not displace the ascending or descending colon toward the midline as the embryomata usually do. However, there is no definite method of always differentiating between these two tumors before operation, nor is it essential to do so, as an operation is required in either case.

Hydro- and pyelonephrosis are also not rare in this age group, and are usually the result of urinary stasis from some congenital malformation. By palpation the hydronephrosis is less solid than the embryoma but this line of distinction is a narrow one at times. If palpation leaves one in doubt, intravenous or retrograde pyelography is clearly indicated. In a case where hydro-nephrosis is suspected the cystoscopic examination with retrograde pyelography and the collection of separate urine specimens are preferred to the intravenous method.

Ovarian tumors, enlargement of the spleen, omental cysts or duplications of the alimentary tract have sufficiently definite characteristics to make their differentiation possible. Among the rarer conditions malignant growth of the liver, congenital cystic kidney, or massive retroperitoneal embryoma, unattached to the kidney, may be difficult to rule out.

The diagnosis of Wilms' tumor having been made, the plan of treatment becomes the important question. Priestley and Broders,⁵ Prather and Friedman,⁴³ Wharton,⁴⁴ Campbell,¹⁶ and many others advocate preoperative irradiation for the purpose of shrinking the tumor followed by a nephrectomy, which is in turn followed by postoperative irradiation. In fact, this plan of treatment may be said to have become the accepted routine in many clinics. Roentgenotherapy usually reduces the size of the tumor very rapidly and thereby facilitates the operation. It does not, however, completely destroy the tumor. No patient, so far as I know, has ever been cured by irradiation alone, and I believe no specimen that has been examined following irradiation has failed to show viable tumor cells. Preoperative irradiation, if used, must be adopted for the purpose of facilitating the operation and reducing the operative mortality, or for preventing dissemination of the tumor.

At the Children's Hospital, in the last ten years, we have had only two operative deaths in 28 cases—an operative mortality of 7 per cent. One of these patients had a very extensive intra-abdominal metastasis at the time of operation and probably should not have been operated upon. The other apparently died of shock. I did not include, as an operative death, a patient who died of acute *Streptococcus meningitis* three weeks after a nephrectomy. The meningitis apparently had no connection with the surgical procedure. Of course, it is possible that preoperative irradiation with the attendant shrinkage of the tumor might have prevented the two operative deaths.

Does irradiation prevent dissemination of the tumor cells? So far as I know, there is no evidence that it does. On the contrary, we have impressions that it may facilitate the spread of the growth. It is the consensus that roentgenotherapy shrinks the tumor by destroying some of the cells but not all

Priestley and Biodeis⁵ state that "In the study of tumors removed at operation which were subjected to preoperative irradiation one may find an island of glandular or sarcomatous-appearing cells growing luxuriantly in the midst of necrotic debris the result of irradiation on surrounding cellular structures" Is it not probable that these living tumor cells may be picked up more readily by the blood stream after irradiation than before it? Our personal experience with preoperative irradiation is inadequate and is limited to but two cases. In one instance it was given for two weeks while waiting for the child to recover from a respiratory infection. The roentgenotherapy was very effective in shrinking the tumor. In this case the child had metastasis to the lungs three months after the nephrectomy and died in eight months with multiple metastases (Figs 6 and 7). In the other instance, roentgenotherapy was advocated by the patient's uncle who was a doctor and was persisted in for four weeks,

FIG 6

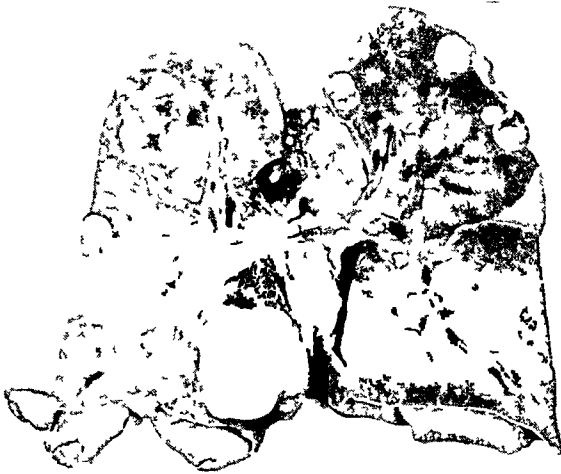


FIG 7



FIG 6—Photograph of the gross section of the lungs (A 37162) of a patient who died eight months after nephrectomy of embryoma of kidney. Pre and postoperative irradiation had been given. Note numerous metastases to both lungs.

FIG 7—Photograph of the gross section of the brain (9A 3762) showing an extensive metastasis in the sulcus of the brain of the patient referred to in Figure 6. Note the hemorrhagic necrosis in the tumor.

at which time the child died before nephrectomy was performed. This latter case was not included in the series of 45 cases, as there was a clinical diagnosis only.

Another fact for consideration is that the number of patients who have apparently been cured to date is not sufficiently large to draw definite conclusions in favor of one plan over another. The number of apparent cures, however, without the use of preoperative roentgenotherapy being greater than those with, suggests the advisability of resorting to operation without delay. As there is no known method of telling when the tumor invades the vascular system, it would seem logical to try to prevent this happening by performing a nephrectomy as soon as possible after the diagnosis is made. The size of the tumor is no criterion of the vascular invasion, as two of our smallest tumors showed the renal vein completely plugged with tumor cells at the time of the operation (Fig 8).

Operative Technique—The question of operability must necessarily be decided on various indefinite factors, the experience of the surgeon, the size of the tumor, and the general condition of the patient. In recent years, at the Children's Hospital, the size of the tumor has in no instance been considered a contraindication to operation. In some instances the weight of the tumor has been as much as one-fourth of the total weight of the child.

The patient is put in as good condition as possible for the operation by the administration of parenteral fluids and transfusion when indicated. In recent years the transperitoneal approach has been substituted for the former posterolumbar incision, as the latter does not give adequate room unless it is carried across the recti muscles and even then, if the tumor be a large one, the approach is less satisfactory. A rectus or a paramedian incision is the one we now employ. After the peritoneum has been opened, the ascending or descending colon, according to the side affected, is reflected toward the opposite side sufficiently to expose the renal pedicle and ureter. These structures are tied and cut before any attempt is made to mobilize the kidney. It is theoretically important to proceed in this order, particularly if the tumor is soft and broken down. The whole mass is then removed, great care being taken not to tear or rupture the capsule. It is probably wise to remove the perirenal fat, particularly along the renal pedicle, as it is here that lymphatic extension is most likely to take place. It is my belief that we have not been sufficiently thorough in this part of the operation at the Children's Hospital. After all bleeding points have been carefully controlled, the abdominal incision is closed in layers without drainage.

The postoperative care has consisted in the administration of parenteral fluids, adequate doses of morphine, and sometimes a transfusion. We have had no difficulty with the wounds made for the transperitoneal approach, even when they extended from the costal border nearly to the pubis.

Until very recently postoperative roentgenotherapy treatment has not been employed. Recently postoperative irradiation has been used on the theory that it may have greater effect on a small amount of tumor that may have been overlooked than on the original, or that some cells left may be of the type that can be completely destroyed by this treatment. The adoption of the present plan of postoperative irradiation is too recent for any evaluation to be made of it.

Prognosis—It is extremely difficult from a study of the literature to draw conclusions as to the superiority of one form of treatment over another. This difficulty arises from the varied nomenclature of kidney tumors and from the lack of follow-up reports or confirmatory pathologic microscopic examinations. One gets the impression, however, from reading some 40 odd articles, that the operative mortality is very high and the late mortality is even higher. In the literature the reports of cures as the result of one form of treatment or another are so few as to be of only suggestive significance.

In a personal communication of November, 1937, Doctor Priestley, of the Mayo Clinic, informs me that they have obtained, apparently, four cures—one

of 17 years, one of six years, and two of three and one-half years' duration. Of these, one had no roentgenotherapy at all, and, including this case, three had no preoperative irradiation. Out of their four cures, only one had had preoperative roentgenotherapy. He had not evaluated the cases operated upon since 1934, and it is possible, of course, that these later results will alter the statistics. Campbell¹⁶ reports one three-year cure that had had no preoperative irradiation and a 15-month cure that had had irradiation. Prather and Friedman⁴³ report one two-year cure following preoperative irradiation and nephrectomy, while Kretschmer and Hibbs⁴⁷ report one cure of one and one-half years' duration which had had nephrectomy only. Mintz¹⁴ has recently reported seven cases of Wilms' tumor occurring in children at the Massachusetts General Hospital. These all died within six months after nephrectomy. Geschickter and Widenhorn¹⁰ report end-results in 25 cases. They state that none of these cases were living at the end of five years, and most of them had died prior to two years after the nephrectomy. McCurdy⁹ reports a series of 24 cases in which there were four operative deaths and a recurrence in the remaining 20. Eleven of these recurrences took place inside of five months. Thus, from the literature one may infer that there were eight probable cures, five of which had received no pre-operative irradiation.

In our series of 45 cases, there are 31 who have died. Of these 31, all but one had a recurrence or had died within one year of the operation. This fact has led us to feel that if a patient survives for more than a year and a half he can probably be regarded as a permanent cure. In the 28 patients operated upon during the last ten years, two died from the operation and 12 died later of the malignancy. Most of these showed evidence of recurrences within six months, and all died within one year after the operation. Of the 14 patients who are still living, 11 may be classified as probable cures, the length of time since nephrectomy varying from one and one-half years to 19½ years (Table I).

TABLE I
THE LATE RESULTS OF NEPHRECTOMY FOR RENAL EMBRYOMA
Without Preoperative Irradiation

Cases	Sex	Age	Nephrectomy	Well after Operation for
1	F	5 mos	Left	7 years+
2	F	12 mos	Right	10 years+
3	M	5 mos	Left	19½ years
4	F	10 mos	Left	3 years
5	F	5½ mos	Left	1½ years
6	F	8 mos	Right	1½ years
7	F	7 mos	Right	4¼ years
8	F	31 mos	Right	13 years
9	M	10 mos	Left	10 years
10	F	5½ yrs	Right	6¾ years
11	M	22 mos	Right	5½ years

The other three patients are not expected to survive. One is the patient mentioned before, who had bilateral tumors and who has had the larger tumor, that of the left kidney, removed, while the embryoma of the right kidney is being treated by roentgenotherapy. This tumor has shrunk so that it is barely palpable, the child looks very well, and has a normal N P N four months after operation. The second patient has had a local recurrence which has been re-operated upon, and all the tumor which could be identified has been removed and the child is receiving roentgenotherapy (Fig 12). The third patient is one in whom it was felt that all the tumor had not been removed at the time of the nephrectomy.

These 11 patients in our series, and eight cases taken from the literature, represent 19 probable cures of embryoma of the kidney. Of these 19 surviving patients, 16 received no preoperative irradiation, while three did. Of course, these numbers are not sufficiently large to be conclusive, but are they not suggestive? Considering the extreme malignancy of Wilms' tumor, and its very early metastasis, is not the chance of obtaining a cure greater by immediate operation than by delaying the operation for three to six weeks in order to shrink the tumor by roentgenotherapy before the nephrectomy is performed?

It is recognized that great strides have been made in roentgenotherapy in recent years, and that it is quite possible that our point of view may soon have to be changed. However, one may also hazard the opinion that it will be difficult to obtain uniform results by roentgenotherapy, on account of the extremely rapid growth, the early metastasis, and the very varied histologic picture which these embryomata present.

A brief summary of selected case reports from our series is appended.

Case 1—I J, female, age 5½, represents a six and one-half year cure following a transperitoneal nephrectomy without irradiation. She was admitted to the hospital June 22, 1931. One week previously, the mother had noticed a mass in the child's abdomen while she was giving her a bath. On close questioning, the mother stated that possibly the child had not had her usual hearty appetite during the past three weeks, but otherwise there were no symptoms.

Physical Examination—She showed some pallor and was slightly undernourished, but there was nothing abnormal in her physical examination or in her laboratory studies except for the abdomen. This was asymmetric, with definite fulness over the entire right side and loin. There was an oval-shaped, firm, nontender, nonmovable, smooth mass, extending from just below the costal margin to the crest of the ilium. Its lateral border extended to the umbilicus, and posteriorly it filled the entire right loin. Its upper edge was separate from the liver.

Operation—June 23, 1931. A transperitoneal nephrectomy was performed through a right rectus incision. The renal pedicle was clamped before an attempt was made to free the tumor. She had a fairly easy convalescence and was discharged on the twenty-first postoperative day with the wound well healed.

Microscopic Examination—The sections were typical of a rapidly growing embryoma of the kidney.

Subsequent Course—In January, 1938, six and one-half years after nephrectomy, her physician reported that she appeared to be in excellent health and had no signs of recurrence.

Comment—A rather typical history of embryoma of the kidney with a six and one-half-year cure following a nephrectomy. This patient received no preoperative or postoperative irradiation.

Case 2—H. A., female, age 7 months, represents a four year cure following a transperitoneal nephrectomy without irradiation. She was admitted to the hospital November 26, 1933. For the past four days she had had a nonproductive cough, fever, occasional vomiting, and constipation. The mother had noticed a mass in the right side of the abdomen one month previously, but at the time of the visit of the family physician this was thought to have been due to bowel stasis. The patient lost one-half pound in weight during the week previous to admission.

Physical Examination—She was a fairly well developed but poorly nourished infant. She was somewhat cyanotic and her respirations were rapid and shallow. The veins of the chest and abdomen were visible. There was evidence of an upper respiratory infection with some bronchitis but no pneumonia. Temperature, 102° F. The abdomen was markedly prominent on the right side. On palpation a tumor was felt that filled the entire right flank. Its upper end was rounded and its mesial border was in the midclavicular line at its upper end, but extended to the navel at its midportion, and was to the left of the midline at its lower margin.

Operation—December 4, 1933. A transperitoneal nephrectomy was performed through a right rectus incision, which extended from the costal border almost to the pubis. The renal pedicle was tied before the kidney was freed. She had an easy convalescence and was discharged on the twentieth postoperative day with the wound well healed.

Microscopic Examination—This showed a typical right kidney embryoma.

Subsequent Course—In January, 1938, four years after nephrectomy, the patient was reported to be in perfect health and to have no signs of recurrence.

Comment—A four year cure of embryoma of the kidney with no preoperative or postoperative irradiation.

Case 3—D. R., male, age 3, presents an early extension of the tumor into the renal vein and an unfavorable prognosis (Fig 12). He was admitted to the hospital November 26, 1937. Four days before admission his mother noticed that he passed some dark colored urine and had some slight frequency during that day. There were no other urinary symptoms. One week before, he apparently had had some abdominal pain unassociated with vomiting, which had lasted for only one day. For the three days before entrance, he had had a rather constant, unproductive cough during the day. There was no fever, anorexia, vomiting, or constipation. He seemed to have no pain, was not fretful, and no physician was called. The mother brought the boy to the hospital for "examination."

Physical Examination—He was well developed and well nourished, and in no apparent pain or distress. The abdomen appeared full in both upper quadrants. There was definite bulging in the right flank where a hard, smooth, nontender mass could be felt.

Operation—December 3, 1937. A transperitoneal nephrectomy was performed through a right rectus incision. The renal pedicle was isolated, and tied before freeing the kidney tumor. The renal vein was dilated and firm to palpation and was ligated close to the vena cava. On section there was evidence of tumor extension into the renal vein. Except for the first three postoperative days he had an easy convalescence.

Microscopic Examination—The sections showed typical embryoma of the kidney with intravascular extension. A section taken from the renal vein showed a rather thick-walled structure, the lumen of which was almost completely occluded by a large mass of tumor cells (Fig 8). A section taken from the pelvis of the kidney including the adjacent portion of the tumor showed marked intravascular extension into the blood.

vessels of the submucosa There was, however, no extension of the tumor through the epithelium of the pelvis

Subsequent Course—Postoperative irradiation was carried out while the patient was convalescing in the hospital He is now receiving roentgenotherapy in the Out-Patient Department There was no evidence of metastasis that could be determined roentgenologically



FIG 8—Case 3 Photomicrograph of section of embryoma of kidney (S 37 483) showing the renal vein filled with tumor cells extending from the main tumor (Hematoxylin and eosin, $\times 18$)

Comment—This case illustrates early vascular extension with the attendant unfavorable prognosis It also illustrates one of the two cases of the whole series in which hematuria was a presenting symptom

Case 4—A M R, female, age $6\frac{1}{2}$, who was the only bilateral case in our series and who had factors which made the diagnosis difficult She was admitted to the hospital January 8, 1938, with a history of abdominal pain and fever of two days' duration

Physical Examination—Showed a moderately ill looking child Temperature, 102° F The general examination was negative except for the abdominal findings In the left side of the abdomen there was a solid, smooth, rounded, nontender and nonmobile mass This could be felt in the left costovertebral angle and extended forward almost to the midline and downward below the level of the umbilicus On the right side, in the kidney region, there was a similar mass except that it was smaller and was tender in the costovertebral angle (Fig 9)

Cystoscopic Examination revealed a very normal appearing renal pelvis on the left, the side of the larger tumor, while on the right the renal pelvis was distorted and displaced toward the midline (Fig 10A and B) The urine examination showed a normal urine from the left kidney and some pus cells in that obtained from the right kidney This case presented a difficult diagnostic problem

Operation—January 27, 1938 An exploratory operation was performed Through a left rectus incision a typical embryoma, of large size, of the left kidney was seen A left nephrectomy was performed The mass in the right upper quadrant was a similar appearing tumor of the right kidney In view of the grave prognosis, it seemed justifiable to obtain a biopsy specimen from the right kidney tumor

Pathologic Examination—*Gross* The left kidney tumor weighed 690 Gm (Fig 11)

Microscopic Examination showed a typical embryoma. The biopsy of the right kidney tumor also showed a typical embryoma. *Pathologic Diagnosis* Primary bilateral embryoma of the kidneys.



FIG 9—Case 4. Photographs showing the outline of the bilateral embryomata of the kidneys, the tumor of the left kidney being larger than the right.



FIG 10—Case 4. (A) Retrograde pyelogram of the right kidney pelvis, the side containing the smaller tumor showing it to be distorted and displaced mesially. (B) Retrograde pyelogram of the left kidney pelvis, the side containing the larger tumor which appears fairly normal.

Subsequent Course—The child made a good postoperative recovery, and is now receiving roentgenotherapy for the right kidney tumor, which has decreased in size until it is barely palpable.

Comment—This is the only bilateral embryoma of our series, and presented unusual difficulties of diagnosis. The normal appearance of the left kidney pelvis after retrograde pyelography and the tenderness in the right side were especially confusing. The prognosis is believed to be hopeless (Figs 9, 10A and B, and 11). Ueda,⁷ of Japan, reports a similar case in an eight months old baby in whom one kidney was extirpated and the child died seven weeks later. In the older literature, frequent mention is made of these tumors being bilateral, notably by Albanian and Imbert,⁴⁵ and Walker.⁴⁶ I have not found such frequent mention of bilateral occurrence in the recent literature.

Case 5—J. M. R., female, age 5 months, illustrates an unusually large tumor, and recurrence and secondary operation following roentgenotherapy. She was admitted to the hospital October 19, 1937. For about two months the mother thought she had felt a mass in the abdomen. This had steadily increased in size. The child had not lost

FIG 11

FIG 12

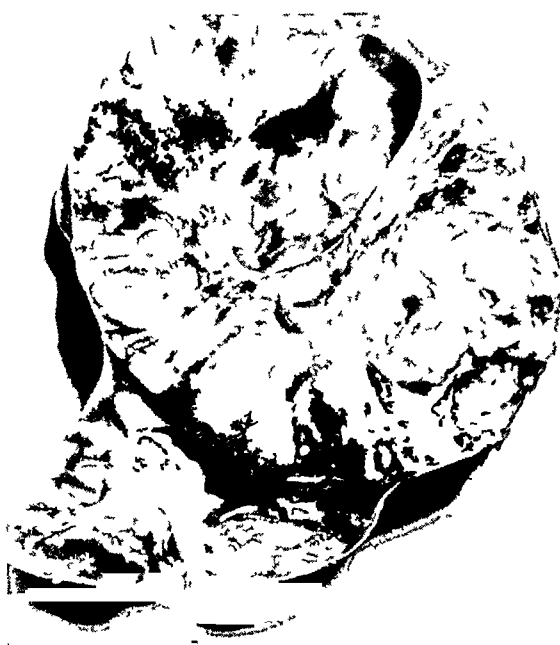


FIG 11—Case 4. Photograph of the gross specimen of the embryoma of left kidney (S 37 31). The other kidney is also the seat of an embryoma. Note large tumor mass separated from the remainder of the kidney by a connective tissue wall. The tumor could not be separated from the rest of the kidney after removal. The cut surface of the tumor is divided into lobules of irregular size. Note small areas of hemorrhage and early necrosis, particularly beneath the capsule. Pelvis of this kidney appeared normal by retrograde pyelography (Fig 10B).

FIG 12—Case 5. Photograph of the gross specimens of the several tumor nodules (S 38 81) which represent local recurrences removed at a second operation, four months after nephrectomy for embryoma of the kidney. Postoperative irradiation had been given.

weight and her only symptom in addition to the mass was that on two occasions during the past week her urine had been dark red in color. There also had been moderate constipation during the last week.

Physical Examination—A well developed and slightly undernourished, rather pale child. The abdomen was asymmetric with a palpable mass in the left side. There was a smooth, nontender mass which filled the entire left side of the abdomen from the costal margin to the pelvic brim and extended across almost into the right flank.

Operation—October 18, 1937. A left transperitoneal nephrectomy was performed through a left rectus incision. The renal pedicle was identified and cut. She had a fairly easy convalescence except for a slight separation of the skin at the upper end of the wound. Two weeks after operation she began to lose considerable weight and she

did not eat well, but following a transfusion she improved, regained some of her weight, and was discharged one month after operation

Pathologic Examination—*Gross* The tumor weighed 1,058 Gm, which was practically one-quarter of the child's weight. *Microscopic Examination* showed a typical embryoma without vascular or pelvic extension

Subsequent Course—For one month after discharge the baby did well, gained four and one-half pounds in weight and was without symptoms. Two months after operation the baby began to lose her appetite and the mother noticed an enlargement in the left upper quadrant and felt a hard mass in this region. She returned to the hospital for further observation

Physical Examination—The abdomen showed a well healed scar. In the left upper quadrant a hard, smooth mass, about the size of an orange, was found which did not move with respirations and which extended back into the left flank. Its lower border was at the umbilicus. There was no tenderness and no spasm. Roentgenologic examination showed no metastasis in the lung, bone, skull or chest. Roentgenotherapy was given and the mass in the left quadrant became very much smaller until it became barely palpable. It seemed advisable to reexplore the patient

Operation—February 24, 1938. Through a left transverse incision, three to four rounded masses, measuring approximately 3 cm in diameter, were found in the kidney bed (Fig 12). These masses were bound to the surrounding structures, namely, the bowel, the lienorenal ligament and posterior abdominal wall. The tumor masses were moved intact. No loose necrotic tissue was noted, though the tumor itself was felt to be necrotic as the result of the roentgenotherapy. She had a rather difficult convalescence and even now we have considerable trouble with her diet and with effecting a gain in weight

Microscopic Examination—The specimen showed a recurrence of the embryoma of the left kidney. On the whole, the sections showed that the tumors were much less cellular, and less rapidly growing than the original one, but still contained viable tumor cells

Comment—This patient is still alive, five months after operation, and without further demonstrable metastasis, but the prognosis is considered extremely unfavorable

CONCLUSIONS

After a study of 45 cases of embryoma of the kidney (Wilms' tumor) occurring at the Children's Hospital, and a partial review of the literature, the appended conclusions are suggested

- (1) That this tumor is extremely malignant and results in a very high mortality
- (2) That the operative mortality has been greatly reduced at the Children's Hospital in recent years
- (3) That the factors contributing to this reduced mortality are better preoperative preparation, better postoperative care, and better operative technic by the transperitoneal approach
- (4) That, to date, more probable cures have been obtained by immediate nephrectomy than by nephrectomy preceded by a course of preoperative roentgenotherapy
- (5) That it is possible that preoperative irradiation facilitates the operation and immediate operative mortality only at the sacrifice of an increased late mortality
- (6) That postoperative roentgenotherapy requires further trial before it can be evaluated

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THERAPEUTIC MANAGEMENT OF URINARY INFECTIONS

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WE HAVE learned to interpret diseases of the urinary tract from the viewpoint of system-physiology and system-pathology, but we have not yet come to employ the concept of system-therapy to their treatment. This is particularly true in the case of urinary infections—where infection of one portion of the urinary tract may quickly involve other portions, or persist in spite of antiseptic therapy if there be faulty urinary drainage.

Any derangement of urinary transposition in any portion of the urinary tract, be it obstructive or functional, will cause infection to persist. In this respect infection in the urinary system differs in its manifestation from infections in other systems of the body.

As an introduction to the present discussion of the therapeutic management of urinary infections, we wish to present a group of cases which should be classified as therapeutic misdemeanors, because in each of these cases some of the underlying principles which should govern the therapeutic management of these infections were overlooked.

Figure 1 is a plain abdominal roentgenogram which shows the end-result of the faulty treatment of a *Proteus* infection in a patient who had but a solitary kidney. We see the left renal pelvis completely filled with stone. Due to the *Proteus* infection, the urine in this patient was persistently alkaline for a number of years in spite of all acidifying medications. In fact, the only time the urine became acid was immediately following a pelvic lavage with 1 per cent phosphoric acid. A plain roentgenogram taken two years previously showed the renal pelvis to be free of stone. During this two year period, however, a large amount of ammonium chloride was given in an attempt to acidify the urine. We know now that this therapy was wrong because the ammonium chloride was merely supplying a large amount of urea to the *Proteus* Bacillus for the liberation of ammonia which encouraged the precipitation of urinary salts. In this case, therefore, we see a failure of our therapy due to the administration of the wrong antiseptic as far as the infecting organism is concerned. We now know that the therapy of choice in *Proteus* infection is administration of sulphanilamide. But at the time when sulphanilamide could be obtained, it was already too late to influence the *Proteus* infection in this case, as the main prerequisite for success in sulphanilamide therapy, sufficient kidney function, was lacking.

Figure 2 shows the intravenous urogram of a patient who had been running a septic temperature for six weeks, with tenderness of the left lumbar region. It was difficult to correlate this excellent visualization of the left side with a septic pyelonephritis particularly in view of the fact that only

occasionally did the urine show any appreciable amounts of pus. More frequently the urine was perfectly clear.

In this patient a retrograde pyelogram of the same kidney showed essentially the same picture as the intravenous urogram. Urine obtained from the ureteral catheter was perfectly clear. When we analyzed these two pictures, however, we realized that, because of good function on the intravenous urogram and the clear urine obtained through the ureteral catheter, it was impossible for this portion of the kidney to be the seat of a septic infection. The only possible explanation was a nonfunctioning, obstructed upper pelvis of this same kidney. That such was the case was proven when the kidney was



FIG 1—Plain roentgenogram showing end result of faulty treatment of a *Proteus* infection of a solitary kidney



FIG 2—An intravenous urogram in an instance of a nonfunctioning obstructed upper pelvis

removed at operation, the upper portion of which was infected, nonfunctioning and obstructed. All the urinary antiseptics administered had been excreted through the normally functioning portion of the kidney. In this case we see a failure of our antiseptic therapy due to a failure of elimination at the seat of disease.

Another problem was that of a man, age 29, with urinary infection plus urethral stricture. At no time had there been any upper urinary tract symptoms, but failure to influence this urinary infection by the various antiseptics, even after the urethral stricture had been sufficiently dilated, caused us to study the upper urinary tract, and in the urogram was demonstrated a full explanation of the reason for our therapeutic failure. It showed a ureteral obstruction on the left due to perimetritis, and inadequate renal function of the right kidney, probably due to the same cause.

Our next therapeutic misdemeanor was in a patient whose only complaint, in addition to his urinary infection, was vague gastro-intestinal discomfort. When the urinary infection did not clear up under the various antiseptics, a

plain abdominal roentgenogram demonstrated a suspicious shadow, which might have represented a calculus in the right upper urinary tract. An intravenous urogram showed a nonfunctioning right kidney, and the plain abdominal roentgenogram, taken with indwelling ureteral catheter (which met no obstruction in the ureter), showed the previous shadow to have moved to a higher position. To complete our diagnosis an air pyelogram was undertaken, which explained completely the failure of the previous therapy as far as the urinary infection was concerned, for here we had a case in which a stone acts as a ball-valve, at times obstructing the outflow of urine at the middle portion of the ureter, at other times resting in the renal pelvis, but at



FIG 3—An intravenous urogram of a female, age 33, showing the pathology consequent to subacute adnexitis



FIG 4—An intravenous urogram of a male, age 31, showing a bilateral peri ureteritis and ureteral dilatation, which has been influenced by adnexal infection

no time causing typical symptoms of an obstructive uropathy, which, had it done so, would, of course, have caused us to make an earlier urographic study of the upper urinary tract. This therapeutic failure was due to delay in performing a complete urographic investigation.

With these illustrative cases as an introduction, let us now consider urinary infection in a more general way. Table I classifies the two principal groups of urinary infections. All infections of the upper urinary tract are secondary to infections elsewhere in the body and depending on their origin, these infections may be classified as (1) primary hematogenous, in which case they remain principally in the kidney, or as (2) urogenous, in which case the infection begins principally in the male or female adnexa but can involve the entire urinary system, producing dynamic disturbances of urinary transportation. Important for us to remember is that if only the peri-urinary structures are involved, the urine will not show any evidences of infection.

Let us take up these urogenous infections more in detail. Figure 3 shows the intravenous urogram of a woman, age 33, who had a subacute adnexitis of three months' duration. At no time were there any upper urinary tract symptoms. In the urine, however, could be found increased evidence of infection. After seeing the condition of the upper urinary tract, it was understood why an infection might persist. Antiseptic therapy was of no avail until the infected adnexa were removed and until, as a result of this, the upper urinary tract emptied itself more completely. Six weeks after a bilateral salpingectomy, a second urographic study showed a remarkable return to normal, and her urinary infection had practically disappeared.

TABLE I

CLASSIFICATION OF THE TWO PRINCIPAL GROUPS OF URINARY INFECTION

All infectious processes of the upper urinary system are secondary to infections elsewhere in the body

- 1 Primary hematogenous
Remain principally in the kidney
- 2 Urogenous
Begin principally in male or female adnexa
Do not remain at portal of entry but involve entire urinary system
Produce principally *dynamic disturbances of urinary transportation*
If only the peri-urinary structures are involved the *urine* will not show *evidence of infection*

The degree to which a restitution of normal physiologic emptying can be attained, in these cases of subacute adnexitis, is related quite definitely to the time element of duration. There is no rest to urinary function, though a very definite limit to reserve power, and if such an obstructive uropathy is allowed to continue, there follows greatly impaired renal function and a true infectious atony of the ureter with gross dilatation of it. Surgery is usually instituted too late to expect anywhere near a return to a normal emptying, and the ablation of the infection is, therefore, not to be expected.

Adnexal disease in the male is too infrequently thought of as a cause of impaired ureteral function and the basis for chronic urinary infection. Figure 4 is an intravenous urogram of a man, age 31. Long standing adnexal infection is expressing itself in a bilateral peri-ureteritis and ureteral dilatation. We have herein a complete corollary to that seen in the female, and it is becoming increasingly frequent as we study, by intravenous urography, cases of chronic prostatitis and seminal vesiculitis with persistent urinary infection. Unfortunately their cure is not so surgically brilliant as in the female, but to halt the advancing damage and destruction of renal function and to obtain a cure of the urinary infection depend upon a prompt recognition of the entire pathologic picture, with persistent and appropriate treatment. It is to be realized that such can progress to the same degree of utter derangement of renal function and a complete futility of all our antiseptic therapy.

URINARY INFECTIONS

TABLE II

POSSIBILITIES OF SEQUELAE OF ADNEXAL INFECTION

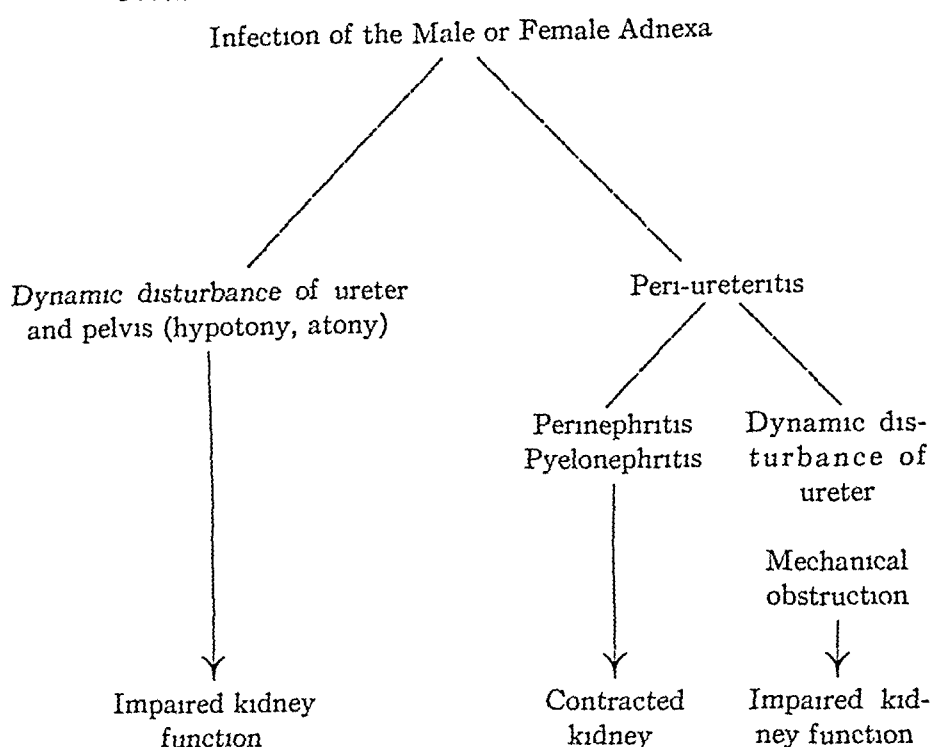


Table II shows a recapitulation of the various possibilities which might occur in infection of the male or female adnexa. The end-result, whether it be through dynamic disturbances or through obstruction caused by a peri-ureteritis, is, of course, the same—impaired renal function.

TABLE III

URINARY ANTISEPTICS

- 1 Oil of santal—Used by Chinese from remote times to treat gonorrhea
- 2 Methenamine—Necessitates urinary pH below 5.6 and concentration greater than 0.5 per cent
- 3 Methylene blue
- 4 Acriflavine
- 5 Pyridium
- 6 Hexylresorcinol
- 7 Ketogenic diet
- 8 Mandelic acid
- 9 Sulphanilamide
- 10 New sulphanilamide substances

Let us now consider urinary antiseptics themselves. Table III gives a very incomplete list of those that may be administered orally, and of these we should consider only those beyond No. 6. We can also dismiss the ketogenic diet, when one realizes that urinary acidification is much more easily obtained by means of mandelic acid. We know that the action of mandelic acid depends on the concentration of the urine greater than 0.5 per cent and

a p_H less than 5.5. We therefore see that the success of mandelic acid depends entirely upon the function of the kidney. Mandelic acid is the antiseptic of choice in *Streptococcus faecalis* infection. Important in a negative consideration is the fact that mandelic acid therapy is useless in *Proteus* infection, as the p_H of the urine in these infections cannot be reduced to the acid side.

The antiseptic of choice, however, in all urinary infections, other than *Streptococcus faecalis*, is sulphanilamide. Marshall and his coworkers found that sulphanilamide is absorbed from the intestinal tract within four hours, and that, in administering a given daily amount of this drug in divided doses, it takes from two to three days to establish equilibrium between the amount ingested and the amount excreted. After equilibrium is established, almost 100 per cent of the daily ingested amount can be found in the urine in the free and combined form. Sulphanilamide is also excreted in the prostatic fluid, and this, of course, makes its use in the urogenous type of infection as invaluable as in the hematogenous type. Almost 50 per cent of the sulphanilamide is excreted in the urine as the inactive acetate. As the efficacy of sulphanilamide depends on the concentration in the urine, it is advisable in the acute urinary infections to limit the intake of fluids to approximately 1,500 cc daily. In acute infections we have obtained the best results with the dosage scheme of 60 gr. a day for three days, with reduction to 40 gr. a day for another four days. But for therapeutic success we need sufficient kidney function. In those cases in which kidney function does not guarantee sufficient urinary concentration of sulphanilamide, we have found it useless to continue our therapeutic regimen beyond a week's time, as outlined above.

For chronic urinary infections, both hematogenous and urogenous, in which kidney function is not markedly impaired, we have not found it necessary to restrict fluids or to administer more than 40 gr. of sulphanilamide daily for a week's time. If there is no improvement in the chronic urinary infection at the end of this period, we are not likely to be therapeutically successful by continuing our therapy longer. We should then look for some asymptomatic obstruction to urinary drainage, or for some fault where failure is due to infectious destruction in whole or in part of a kidney.

Sulphanilamide possesses a great advantage over mandelic acid in that it is efficacious in alkaline urine. In fact, it is more effective in a slightly alkaline urine, as Helmholz has shown. This makes sulphanilamide particularly valuable in *Proteus* infections.

In summary, therefore, we may say that our therapeutic management of urinary infections calls for the use of mandelic acid in *Streptococcus faecalis* infections and the use of sulphanilamide in all other infections, but that the ultimate success depends upon three essential criteria, which must be known, namely: First, knowledge of the type of infecting organism, second, the presence or the absence of faulty drainage, third, that competent renal function conveys the appropriate antiseptic to the desired point.

DISCUSSION—DR BOLAND HUGHES (closing) When a substance such as sulphanilamide is introduced into medicine, one eventually passes through the stage of enthusiasm to that of confusion, confusion because following the original discovery, many allied substances are presented, each purporting, apparently, to possess some advantage over the original product itself

We have been experimenting with several substances in the clinical investigation of urinary infections. Doctor Marshall has found di-sulphanilamide to possess a therapeutic index five times that of sulphanilamide itself. It is slightly less soluble in water but possesses the advantage of being excreted in the urine in the unaltered form. However, as far as urinary infections are concerned, we have found di-sulphanilamide to be superior to sulphanilamide only in pseudomonas infections. In a series of 53 cases treated with this substance, we found that two of our patients developed symptoms of peripheral neuritis. This, of course, indicates the great difficulty in transcribing, immediately, results as obtained from mice to man, because we can understand how difficult it might be to diagnose peripheral neuritis in the mice we infect and then treat with our drug.

We are also investigating the sodium salt of di-sulphanilamide. We have treated only 15 cases, and it may be that the sodium salt will not cause the symptoms of peripheral neuritis such as are obtained from the use of di-sulphanilamide itself.

However, no matter what urinary antiseptic we employ, be it either sulphanilamide or some new substance, which proves to be efficacious, we must recognize the three cardinal principles that Doctor Randall has mentioned in the present communication, namely of knowing the infecting organism, of being certain that the kidneys function sufficiently to excrete the urinary antiseptic employed, and of correcting urinary stasis if present.

THYMOL THERAPY IN ACTINOMYCOSIS

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So-called lumpy jaw in cattle was first described by LeBlanc (1826), who, however, failed to understand its true nature. Although 50 years later Perionito (1879) claimed priority for the discovery of actinomycosis, he was antedated by Bollinger (Munich, 1877), who described a series of pathologic processes of the jaws and throats of cattle which had previously been considered as osteosarcoma, bone cancer and wooden tongue. Bollinger demonstrated the granulomatous nature of the condition and described detritus containing granulation cells, leukocytes, and opaque, yellow granular bodies which he regarded as true fungi. While these observations of the disease in cattle were being made, Lenert (1846) and von Langenbeck (1848) had described similar lesions in man. Later, James Israel (1879), working independently, recognized and described a fungus, found in a case of chronic empyema in a man, in which there was a large thoracic abscess present, as being similar to that found by Davaine (1859) and Bollinger (1877) in cattle. However, while these various studies concerning the "sulphur granules" in relationship to actinomycosis were frequently made, the botanist, Haiz (1877-1878), was the first to call them ray fungus, or actinomycosis.

While such studies were mostly being made in Europe, John B. Murphy was the first (1885) to report an instance in a human being in the United States. About this same time Oscar Israel (1884) and Bostroem (1891) were making further observations as to the characteristics of the fungus. They found it to be aerobic. This concept, however, was overthrown by the work of Wolff and James Israel (1891), who demonstrated the cultures of *Actinomyces bovis* to be anaerobic. This view, which was confirmed by Wright (1904-1905), is the one held at the present time, although the question is still not definitely settled. Liguieres and Spitz (1902) described the bacillary form.

Etiology—While there is some confusion as to the nature of the organism and its variability, it is generally recognized that the anaerobic *Actinomyces bovis* is most commonly responsible for the infection in man and appears to be the sole organism capable of producing the "sulphur granule." The only other organisms causing confusion are those found in instances of Madura foot (aerobic *Actinomyces farcinicus*), a few scattered instances of the occurrence of the *Actinobacillus*, and *Actinomyces comitans* found in four human cases in Zurich. Although there is much confusion in terminology in various grossly related pseudofungus forms and other terms, such as *Nocardia* and *Streptothrix*, which are frequently used, the term actinomycosis

is the oldest, best established, and most accurately conveys the character of the disease in man and in animals

Transmission—There are two common theories (1) Exogenous theory—The agent is considered a common parasite of the vegetable world living on grasses and cereals and is introduced by them mechanically. In some instances seeds and blades of grass have been found in the lesion. (2) Endogenous theory—This is the most widely accepted. Since *Actinomyces bovis* does not form spores, is anaerobic, and apparently grows only at body temperature, it could not exist in the plant world. The organism is occasionally present in the alimentary tract as the result of ingestion. Fragments of teeth are frequently found in actinomycotic lung abscesses, the disease occasionally develops in the knuckles after striking an adversary's broken tooth, or may develop following tooth extraction. Workers have isolated anaerobic strains of *Actinomyces* from the mouth, tonsillar crypts and in the tartar around teeth. The botanical position of the fungus is still unsettled.

Diagnosis—Although the diagnosis may be made from the tissues and microscopic sections, it is more easily and best made by examination from the pus from the discharging sinuses. The "sulphur granules" are readily recognized. They may be studied (a) as fresh preparations under the coverslip, (b) stain from mycelium, (c) may be cultured in various media.

Incidence—Actinomycosis is a widespread disease occurring in all parts of the United States, being most common, however, in the Mississippi Valley and in the Northwest. The distribution corresponds somewhat to the dairy industry, and the association of man with cattle. It is most frequently found in males (80 per cent) between the ages of 20 and 30 years, with instances having occurred as early as 28 days and as late as 82 years (Sanford). Jacobson states that the cases are most commonly seen in the third and fourth decades. In the period between 1899 and 1906, Ruhrah collected 62 instances of actinomycosis in this country. In 1922, Sanford and Magath reported 96 at the Mayo Clinic, in addition to 119 found in the literature. In 1923, Sanford, in a careful review, was able to find a total of 678 cases in this country, but concluded that these probably represented only a small proportion of the true number.

Anatomic Location—Although the disease process in man may be found in various parts of the body, as in cattle, the lesions are most commonly found in the head, and diminish in frequency as the caudal end of the body is approached. Accordingly, 60 per cent are found equally divided between the jaw, neck and face, 18 per cent are abdominal, including wall, peritoneal cavity, liver, intestine and appendix, 15 per cent are in the thorax, including the chest wall and the lungs, less frequently in the ribs and mediastinum, while only 8 per cent are found in the skin, and the disease is seldom found in bones other than the jaw.

Pathology—Actinomycosis may be acute, subacute or chronic. It differs markedly from tuberculosis and syphilis in that it tends to remain localized and spreads only by direct continuity, its dissemination being largely due to

inhalation and ingestion. Its extension through the lymphatics is not recognized, but instances of rupture of the process into blood vessels with distant metastases have been reported. The lesion is initiated primarily, following the traumatic introduction of the organism, as a firm mass which gradually softens and breaks down. Various tissue planes are successively destroyed and replaced by granulation tissue, containing multiple abscesses. A very marked fibrous tissue reaction may occur, giving rise to a brawny induration of the skin overlying the lesion. However, the external aspect usually presents edema, erythema and multiple sinuses.

Microscopically the lesion appears granulomatous in nature but varies considerably according to the amount of secondary infection present. Typically, masses of radially branching mycelial filaments surrounded by lymphocytes and large mononuclear cells are seen. Beyond this a rather well marked fibroblastic reaction frequently containing giant cells is noted. Examination of the discharge reveals a thin, purulent exudate, usually containing the minute yellow "sulphur granules." The organisms are much more frequently demonstrated in the exudate than in the tissue.¹⁵

Treatment—Although the etiology and the pathology have been known for some time, the futility of the treatment has always been recognized. Formerly it consisted of (1) radical surgery, drainage and curettement, (2) roentgenotherapy, (3) iodides in massive doses (400 drops of KI t.i.d.), (4) copper sulphate, gr $\frac{1}{4}$ (Bevan), (5) colloidal gold, (6) colloidal copper injections, (7) attempts at the elevation of metabolism by intravenous glucose with one unit of insulin for every 3 Gm sugar, (8) methylene blue, (9) autogenous vaccine, and (10) nonspecific protein therapy. In recent years, however, this extensive array of methods has been simplified so that at the present time the following methods are employed: (1) Radical surgery, either alone or combined with iodides, (2) iodides alone, (3) roentgenotherapy, and (4) thymol with surgery.

Thymol Therapy—Perhaps the greatest advance in the treatment of actinomycosis was made when the fungicidal action of thymol was first demonstrated by Kingery and Thienes⁶ (1925), who reported a yeast-like dermatosis of the hands in fruit packing plant workers in the Northwest.

Myers and Thienes,⁷ in June, 1925, treated a case of the above with 10 per cent alcoholic solution of oil of cinnamon. This oil was employed because of its efficacy against mold growths in preparations such as infusion of digitalis. Many cases were treated with this, and cinnamon water was used prophylactically. This led to investigation of comparative toxicities of several volatile oils and stereoptins on cultures of the pathogenic yeast responsible for these infections. Experiments with 12 volatile oils proved thymol to be the most efficacious in destroying the yeast. Following this experiment, a mixture of 5 per cent thymol and 2 per cent cinnamon was painted on sites of infections and appeared to effect rapid healing. Further employment of this mixture was made in instances of epidermophytosis infection of feet, pulmonary mycosis, low grade infections of extremities and finally in a case

of cervicofacial actinomycosis, which was treated with doses of thymol orally twice weekly, starting with 0.5 Gm and ending with 1.5 Gm with definite improvement.

Myers,⁸ in 1927, further reported on "an unappreciated fungicidal action of certain volatile oils." He experimented with 22 volatile oils and found thymol and carvacrol, its isomer, the most effective both clinically and experimentally. A culture of actinomycoses proved readily susceptible to an aqueous solution of thymol but was resistant to the other oils. He concluded that powdered thymol in capsules by mouth was absorbed and circulated in sufficient strength to have pronounced fungicidal effect upon two patients with pulmonary moniliasis and one with actinomycosis; also he felt that localized, superficial mycotic infections may be treated with solutions of the oils and thymol in either alcohol or olive oil, in strengths compatible with the local irritability of the tissues.

Our method of procedure in the few cases has been to give orally 1.5 Gm of powdered thymol in capsules two out of every three days, to open the sinuses widely, and to curette and fill them with thymol in olive oil (10 per cent solution), and then to inject the sinuses each day, small strips of gauze being inserted to keep them open.

CASE REPORTS

Case 1—E. M., male, age 63, common laborer, was admitted to M. C. H. August 7, 1934, with a draining sinus in the right upper jaw which on entrance was thought to be due to an infected molar tooth. This was drained but continued to discharge. The patient was discharged but was readmitted September 25, 1934, with enlargement of the posterior aspect of the right side of the neck, having several draining sinuses under the right mandible. Eight days later the sinuses were curetted, on the same day thymol was started by mouth and the sinuses were injected daily with a solution of 10 per cent thymol in olive oil. At this time actinomyces were identified in the curetted material. The injections continued for ten days and given by mouth 21 days, when he was discharged. The patient received a total of 58.5 Gm of thymol by mouth, or an average daily dose of 0.86 Gm. From the time of thymol treatment until discharge there elapsed a period of 51 days. He was followed in the Out-Patient Clinic for several months, and was reported clinically cured.

Case 2—J. N., white, male, age 59, blacksmith, a habitual chewer of straw, was admitted to the hospital August 10, 1924, with a swelling under the right mandible. The diagnosis of osteosarcoma was made and high voltage roentgenotherapy was instituted. The lesion, however, continued to increase in size and on September 15, 1924, it was incised. Staphylococci were identified. However, the diseased condition continued to increase and on December 24, 1924, actinomyces were identified microscopically. Potassium iodide, up to 250 gr. a day, was given by mouth over a period of 58 days. This was then discontinued and thymol therapy, consisting of 1 Gm by mouth twice weekly, was instituted. Seventeen days following the beginning of thymol therapy, the swelling had decreased markedly in size, and the dosage of thymol was increased to 1.5 Gm twice a week. On April 25, 1925, the patient was discharged without evidence of a draining sinus. He, however, failed to return for check-up in the Out-Patient Clinic, so that the final outcome is not known.

Case 3—A. S., male, age 45, farmer, was seen in April, 1925, with a discharging abscess under the left mandible, which he had noticed for two months. Actinomyces

were identified Thymol, 15 Gm in capsules on alternate days was administered Within one month the lesion was completely healed and his family physician reports that there is no evidence of recurrence

Case 4—J L was first seen as an outpatient in St Vincent's Hospital in 1930, with a draining abscess under the left mandible Microscopic diagnosis of actinomycosis was made Thymol was started by mouth and after a period of 12 weeks the lesion had completely healed without any evidence of recurrence

Case 5—E H, male, age 30, farmer, was first seen in September, 1937, at which time he had three draining sinuses in the region of the left jaw Six months previously he had gotten a "grass seed" lodged in his left ear, this was followed by a painful swelling in the left side of the neck Removal of the grass seed afforded temporary relief of the pain but did not result in any change in the mass present Three months later this mass was drained, resulting in the sinuses seen on admission to the hospital

A large mass with several draining sinuses was present below the left mandible and in the region of the left parotid gland The patient was unable to open his mouth more than about one-fourth of an inch at the incisors The purulent material obtained from the sinuses showed typical "sulphur granule" bodies and actinomycoses were identified

He was placed on thymol by mouth 0.5 Gm t.i.d. for two consecutive days with one day of rest This was continued for ten dosage-days, to a course which was then followed by a week's period of rest The lesions showed no evidence of improvement In November, 1937, the sinuses were widely opened and packed with gauze saturated in 10 per cent thymol in olive oil Following this the tracts were again opened and curetted on five different occasions Daily irrigations and packing the tracts with the above mixture were maintained In February, 1938, due to slow progress, he was given a course of six roentgen treatments over the affected area This was followed by marked but temporary improvement Since that time several new abscesses have formed and been drained At present he has six sinuses Since the last surgical procedure the cavities have continually diminished in size and capacity He has maintained the above schedule of oral administration of thymol to date with no apparent ill effects His urine is normal

Case 6—Although not a case of cervicofacial actinomycosis, this case belongs to the cutaneous group, and is included through the courtesy of Doctors Hunter and Holden

M L, white, female, age 40, was first treated March 21, 1936, for an inflammation of the left shoulder, which was considered at first to be erysipelas, after several days it had spread rapidly toward the neck, the left breast, and then the left arm On April 18, 1936, actinomyces were identified microscopically from the pus obtained On April 21, 1936, the patient was placed on a regimen of 2 Gm of thymol a day by mouth, and a 10 per cent solution of thymol in olive oil was injected into the sinus The thymol dosage was decreased to 1 Gm a day on June 21, and discontinued on August 24, 1936 On September 10, 1936, the sinuses were thoroughly curetted These healed quite rapidly and there has been no further evidence of infection

CONCLUSION

A review of previous methods of treatment as compared with the experience at the University of Oregon Medical School and St Vincent's Hospitals, following the introduction of the use of thymol by Doctor Myers and his associates, as well as my own limited experience, leads me to the conclusion that the most effective present day treatment of actinomycosis is a combination of radical surgery with thymol

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DISCUSSION —DR OWEN H WANGENSTEEN (Minneapolis, Minn) As Doctor Joyce pointed out, the etiology of actinomycosis is largely an enigma There are those who insist that the disease is endogenous in origin, that is, that most of us carry about with us in health, organisms within our mouths which, under provocative circumstances, may give rise to the disease, actinomycosis I do believe, however, that the majority of men who through experience and interest have acquired more than an ordinary acquaintance with the subject still subscribe to the old and more orthodox idea that the anaerobic *Actinomyces bovis* is the usual causative agent of actinomycosis

Dr A T Henrici, Professor of Bacteriology in the University of Minnesota Medical School, who as many of you know is an acknowledged authority of the higher fungi, has been kind enough to examine for me the material removed for diagnostic purposes or at operation from suspected cases of human actinomycosis In all instances in which Doctor Henrici was able to establish the presence of actinomycosis he found that the cultural and morphologic characters of the organism were those of the anaerobic, gram-positive *Actinomyces bovis*

As Doctor Joyce also pointed out, actinomycosis is essentially a granulomatous process in which the evidence of both an acute and chronic infection

occurs concurrently Centrally areas of necrosis, liquefaction, and abscess formation may be found, more peripherally a proliferative reparative process occurs in which large collagenous fibers of connective tissue may be found—an attempt on the part of the host to arrest the spread of the disease These areas of softening and induration are interspersed, which accounts for the brawny induration between and peripheral to the abscesses The reddish violaceous appearance of the skin together with the unusual texture may give the impression of a carbuncle

The anaerobic *Actinomyces bovis* live and thrive in the dead and dying detritus of the central areas of softening and abscess formation The macrophages of the host constitute a means of spreading and extending the disease by carrying the organisms into adjacent healthy tissue

With the consideration in mind that the areas of abscess formation, without blood supply and without oxygen, constitute an excellent medium for the perpetuation of the disease, it is quite obvious, I think, what the therapy indicated should be The most direct method of attacking actinomycosis in man is to exenterate all the dead tissue by curetting it away If that is done the spread of the disease will be arrested The disease thrives only in tissues in which the oxygen tension is low

When Doctor Joyce acquainted me, somewhat more than a year ago, with the experience which he and his colleagues had had with the treatment of actinomycosis with thymol, I was anxious to give the method a trial and tried to carry it out as he had used it However, I was not so successful with its use as he, and after indifferent results in two cases, gave it up in favor of curettement

Doctor Joyce reported the use of thymol in six cases of actinomycosis In two of these, thymol had been used as the sole therapeutic agent, in the other four, surgery as well had been employed It is, of course, quite significant that Doctor Joyce has been able to cure two cases of actinomycosis with thymol alone In this connection it is to be borne in mind, however, that spontaneous fistulization alone succeeds occasionally in curing benign forms of the disease

In the surgical clinic at the University of Minnesota, I set out, in 1929 and 1930, to determine which of the therapeutic agents which were in common use (surgery, potassium iodide, and irradiation) in the treatment of actinomycosis was most effectual The experience of our clinic with a combination of these agents had not been a happy one Surgical measures seemed to be the most direct approach, so I began with that method first The results were so satisfactory and so much better than had been achieved by half hearted surgery in association with oral administration of large doses of potassium iodide and external irradiation that I never got around to test the efficacy of these latter agents as sole therapeutic measures Since 1930, therefore, all cases of cervicofacial actinomycosis have been treated by surgery alone In the beginning, actinomycotic lesions were excised, but I soon learned that mere curettement and keeping the wound open by packing were just as effectual During these years a large number of cases of actinomycosis have been seen and only one case of cervicofacial actinomycosis has died (ref Table I, Case 3, *ANNALS OF SURGERY*, 752, 770, 1936) The lesion had extended through the orbit and auditory meatus into the meninges

In most instances two curettements have sufficed In one very extensive case (E E Univ Hosp No 663102) involving the entire right side of the face and neck, six curettements were necessary A few patients with chronic

granulomata, in which the diagnosis of actinomycosis could not be established, have been treated by curettement also, and with equal success

Surgeons are no more objective than other medical men and though we find pleasure in wielding the weapons of our armamentarium in the practice of our art, yet should actinomycosis or any other disease prove equally or more responsive to treatment by nonsurgical means, I am certain surgeons would be the first to acknowledge the superiority of nonoperative treatment. Until such a remedy for actinomycosis is found, however, the most direct attack possible should be made upon the disease, namely, exenteration of the dead tissue.

I cannot conclude this discussion without saying something of potassium iodide, and roentgenotherapy in the treatment of actinomycosis. The use of potassium iodide originated from veterinary medicine. It has since been learned, however, that potassium iodide has no virtue in the management of real bovine actinomycosis. For actinobacillosis which causes "woody-tongue" in pigs and simulates actinomycosis closely from a pathologic standpoint, potassium iodide is a specific. Actinobacillosis, however, is apparently extraordinarily uncommon in man and its occurrence has been reported only twice.

Those of you who have followed the work of Heyerdahl in Oslo, employing roentgenotherapy in the management of actinomycosis, know that the method has merit. Yet the method appears to be valuable insofar as it promotes fistulization and encourages external drainage of the detritus in the diseased process. It is my impression that practically every case of cervicofacial actinomycosis can be cured if direct rather than dilatory approaches to the disease are employed.

THE PROBLEM OF WOUND HEALING

THE EFFECT OF LOCAL ANTISEPTIC AGENTS ON INFECTED WOUNDS

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THE history of the surgical art is replete with changing fashions in the management of wounds. At a time when the current practice demanded relentless, drastic treatment of wounds, Paracelsus aroused a conflict with the contention, " 'Tis Nature healeth wounds, not meddling " Our knowledge of wound healing has improved vastly since the sixteenth century, but the conflict that developed at that time still remains unsettled. The state of antiseptic nihilism which existed prior to the World War¹ was followed shortly by a period during which the surgical literature was flooded with reports of new and different agents supposed to hasten the healing of wounds, and we are still in this phase of the cycle. The fact that there still exist differences of opinion as to the proper management of infected wounds is an evidence that the fundamental problems have not yet been solved.

It is the purpose of this communication to consider further the problem of wound healing, with particular reference to the effect of local agents upon infected wounds in man. Quantitative methods have been employed in this study, and clinical impressions, which are so often misleading, have been avoided.

The gross and histologic phenomena of wound repair are now well understood. The nature of the stimuli which initiate the mechanism of structural repair, and the factors, local and remote, which may alter the process are not so clearly understood. The reparative stimuli or growth-promoting substances which activate the structural mechanism of wound repair are, at least in part, the products of cell destruction, resulting directly or indirectly from trauma.² These substances, which are closely related to certain protein decomposition products, are elaborated by leukocytes and are abundantly present in embryonic tissue juices.^{2, 3, 4, 5} The work of Hammett and Reimann,⁶ Hammett,⁷ Reimann,⁸ Baker⁹ and Birnbaum,¹⁰ suggests that the growth-promoting hormone may be a chemical agent containing the sulphydryl group.

Whatever may be the exact nature of the reparative stimuli, and the forces which condition healing in a wound, it is important from a practical standpoint to understand the normal rate of healing in order to determine variables which may speed or retard tissue repair. Carrel and his associates afforded a quantitative approach to the problem from studies of the surface area of superficial, surgically clean wounds in man and animals. Carrel and DuNouy^{11, 12, 13} demonstrated that clean superficial wounds cicatrize according to a regular

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geometric curve, which may be expressed by a mathematic equation in function of area and time. The curves of wound healing which they presented, indicate that the rate of healing is proportional to the area of the wound and decreases with the age of the patient. These investigators also demonstrated the existence of a latent period, during which no decrease in the size of the wound occurs, normally varying from two to five days following the creation of the wound¹⁴. A latent period of four days from the time of incision to the abrupt onset of fibroplasia, has since been observed by Howes and Harvey¹⁵ in an experimental study of gastric incisions in rats.

The latent period and the rate of healing after the actual onset of fibroplasia may be affected by many factors, local or remote. Arey⁵ has recently reviewed the entire literature on this subject. A brief summary, however, of the factors which are definitely known to influence wound repair is appropriate to this discussion, in order that the many variables may be kept in mind.

Factors of a general nature, not applied or localized directly at the site of the wound, which may influence healing are: Age, diet, distant infection, and hormones. The experimental work of Carrel and DuNouy¹⁴ and the later observations of Howes and Harvey,^{15, 16} have established the fact that the rate of healing is inversely proportional to the age of the patient. Howes and Harvey tested the tensile strength of gastric incisions in rats at varying intervals and noted the earlier onset of fibroplasia in younger animals. They could detect no difference in the velocity of healing, once growth had been initiated, although there was less tendency to retardation of repair in young animals. Carrel and DuNouy, however, measuring the surface area of superficial wounds in man and experimental animals, observed a more rapid rate of cicatrization in younger individuals throughout the entire course of wound repair.

Clark,¹⁷ using the technic developed by Carrel, found that a high protein diet shortened the latent period of superficial wounds in experimental animals, but did not influence the rate of healing after the onset of repair. On the other hand, Howes and Harvey¹⁸ observed no difference in the length of the latent period in animals on a high protein diet, but the velocity of fibroplasia was increased and gastric incisions in rats attained a maximum tensile strength more rapidly. The above observations differ as to the exact phase of healing influenced by a high protein diet, but agree that a high protein diet shortens the total time required for wound repair, and that the course of healing is in some way influenced by protein metabolism. Recent work by Ravdin and Thompson¹⁹ demonstrated the retardation of healing of abdominal incisions in dogs with experimentally induced hypoproteinemia. Normal healing was attained after restoration of normal serum protein concentration through the use of lyophilized serum.

Changes in the carbohydrate intake, according to Clark, do not influence the rate of healing of superficial noninfected wounds. Considerable experimental evidence exists, however, to indicate that high carbohydrate diet, and

disturbances in carbohydrate metabolism, unfavorably influence the course of cutaneous infections²⁰ Absolute starvation did not appreciably alter healing in the experiments of Howes and Harvey,^{15, 21} unless the nutritional balance was disturbed to such a degree that it, in itself, threatened survival

Investigation of accessory dietary factors—the vitamins—indicates that vitamins A and C are of particular interest in relation to the problem of wound healing⁵ Avitaminosis generally tends to retard healing, and over-dosage of vitamin D has been claimed to inhibit tissue repair, but the effects of vitamins A and C are more specific An A deficiency, which has existed over a long period of time, delays wound repair Treatment with vitamin A is said to accelerate healing under such conditions, even when employed locally, and may possibly influence healing in the absence of pronounced deficiency The experimental and clinical studies of Lanman and Ingalls²² indicate that vitamin C deficiency is of particular significance in wound healing They demonstrated, quantitatively, lowered tensile strength of wounds in partially scorbutic animals and emphasized the fact that asymptomatic scurvy, detectable only by plasma determination of ascorbic acid, is of more importance in the healing of surgical wounds in humans than has been hitherto appreciated These findings have recently been confirmed by Taffel and Harvey²³

Through clinical observations, and a few experimental studies, attempts have been made to correlate the functions of the various endocrine glands with tissue repair No significant conclusions, however, can be drawn from the available data, other than that the possible effect of the endocrines must be considered in an occasional case wherein healing has been delayed

Carrel²⁴ demonstrated that retarded healing may result from the presence of a distant infection experimentally produced, supporting a common clinical observation on the influence of remote infection on wound healing There is some evidence to support the belief that general infections, particularly syphilis, retard healing irrespective of their influence on the general health of the patient²⁵

Infection, mechanical or chemical irritation, temperature and blood supply of the part, and local therapeutic agents must be considered as factors acting directly at the site of the wound which may influence healing Carrel²⁶ demonstrated that experimental wounds in animals failed to heal when completely protected from local irritation Mild infection and irritation initiate cicatrization, but gross infection or local trauma from mechanical or chemical irritation retard healing, according to the observations of Carrel¹¹ and Howes and Harvey¹⁵ Delayed healing from diminished blood supply is a familiar observation in occlusive peripheral vascular disease, whereas, increased blood supply and local temperature elevation favor healing of indolent ulcers⁵ Less attention has been directed toward differences in local blood supply of various types of tissue in relation to wound healing

The effect of local therapeutic agents is more difficult to evaluate Good results have been claimed for many forms of radiant energy, roentgen rays and other physical agents Local application of hormones and vitamins has

been advocated. Stimulants containing the sulfhydryl radical, embryonic extracts, allantoin, and urea have all been proposed for local treatment of wounds. Numerous chemical agents, to be used as stimulants or antiseptics, are in common use, each having its own enthusiastic group of supporters. It is apparent from a survey of the literature that doubt must still exist concerning the claim of this horde of vulneraries because of lack of quantitative data. Many of the reports of common local therapeutic agents are merely enthusiastic clinical impressions. Studies based upon the healing time of a series of similar wounds do not take into consideration the many variables which may affect healing. A large majority of reports do not contain accurate bacteriologic studies. The early, incidental observations of Carrel,¹¹ and the recent critical work of Smelo,²⁷ are the only strictly objective studies that we have found on the subject of local therapeutic agents in relation to wound healing. Carrel¹¹ noted that gross infection retarded healing of superficial experimental and surgical wounds, and secured normal healing curves by using antiseptic dressings of dichloramine-T or Dakin's solution. Smelo, in a quantitative study of surgically clean wounds in man, observed the effect of many local agents, with particular reference to the supposed tissue stimulants. No local agent was found to influence the rate of repair in a consistent manner. He concluded that a wound will heal or fail to heal regardless of the material applied locally.

As many pertinent questions remain unanswered it is our purpose to consider further the quantitative effect of local agents, particularly the antiseptics, on the rate of healing and the bacterial flora of frankly infected wounds, whether superficial or deep. Is it possible to substantiate the frequently implied contention that antiseptics further repair by exerting a selectively greater effect on bacteria than on tissues? Is the chemical irritation from antiseptics in common use sufficient actually to inhibit the processes of repair by their lethal effect on the tissue cells? Will the topical application of any of the commonly used germicides actually result in wholesale destruction of virulent bacteria *in vivo*, and if so, will the change thereby produced in the bacterial flora appreciably alter the rate of wound healing? Will local agents, applied to the surface of a wound, prevent further tissue destruction and retardation of repair in the presence of infection with virulent, invasive organisms?

METHODS EMPLOYED—In an attempt to ascertain the exact value of topical agents in the treatment of infected wounds, precise measurements were made of changes in the size and bacterial count of twenty wounds. The wounds studied differed in size, etiology and bacterial flora, but each was of the type regarded as surgically infected. It is important to stress the fact that all of the wounds under consideration were adequately drained. Improper drainage admittedly retards healing and evaluation of any methods of therapy in a series of infected wounds would be questioned if the sound principles of adequate surgical drainage had not been applied to all cases. The patients were in good health, unless otherwise stated, and every effort

was made to determine the presence of any factor, remote from the site of the wound, which may have unduly influenced the local changes. The dressing and management of these cases during the period of observation, and the quantitative studies of the wounds were carried out personally by the writer. Each wound treated with an antiseptic agent was dressed daily.

The surface area of superficial wounds was determined by the technic described by Carrel¹¹. Since the writer was primarily interested in infected wounds healing by granulation, particular attention was directed toward changes in the volume of the wounds, rather than to changes in the surface area. Volume was determined by making a mold of the wound, using a sterilizable moulage which could be trimmed to conform to the contour of the body at the surface of the wound. The mold thus obtained could be easily removed, without trauma, and the volume determined with a minimal experimental error, even in deep wounds with overhanging edges. This method was used in a previous study reported from this laboratory.²⁷

Quantitative bacteriologic study of these wounds presented a more difficult problem. Previous investigators of wound healing have contented themselves with occasional cultures or, at best, with bacterial counts by direct smear from the wound. Such direct smear counts are grossly inaccurate²⁸ and do not give a true picture of the bacterial changes in the entire wound. We have found not only differences in the bacterial count, but also variations in the type of organisms from smears or cultures in separate portions of the same wound. Washing the entire wound with a small amount of normal saline, the quantity being roughly proportional to the size of the wound, afforded a means of obtaining a fairly representative bacterial count. No attempt was made to compare the bacteriologic changes in different wounds, quantitatively, but the changes in any given wound, from day to day, could be followed with reasonable accuracy by using the same amount of saline for each washing. The decrease in the size of the wound as healing progressed would, in itself, tend to decrease the bacterial count of the standard volume of saline, and as a source of error would tend to favor the antiseptic agent. Hence, the failure of an antiseptic agent under investigation to decrease the count would further emphasize the impotence of that particular agent. The actual count was obtained by the dilution method, using as a rule one cubic centimeter of the washing from the wound, and employing dilutions of 1 + through 15 tubes, with vigorous shaking between transfers. This technic is admittedly unsatisfactory for use in certain types of laboratory investigation,²⁹ but has proven satisfactory for our purposes in clinical use, where only gross changes are considered to be of significance. The dilution method also minimizes any effect, *in vitro*, of small portions of antiseptics carried over in the washings, and has the advantages of a technic which permits counting of only the living organisms. No deleterious effect was noted from the use of saline as the diluent, as is true in laboratory work,²⁸ probably because of the admixture of serum from the wounds. In spite of this, however, the washings from the wounds were not allowed to stand over two hours before

making the transfer to the culture media for the serial dilutions Neopeptone, meat infusion broth, buffered to pH 7.3, was used in all the dilutions. Final readings were made only after 48 hours of incubation, the logarithm of the dilution of the last tube showing growth being recorded. Dilutions were made in duplicate on cases early in the series, until it was well established that the technic afforded a method of study with little experimental error. Aerobic and anaerobic cultures, in broth and on blood agar plates, were made of each wound at the start of the period of investigation, in order to identify the types of organisms present. These were repeated whenever a change in rate of healing suggested the possibility of a qualitative change in the flora.

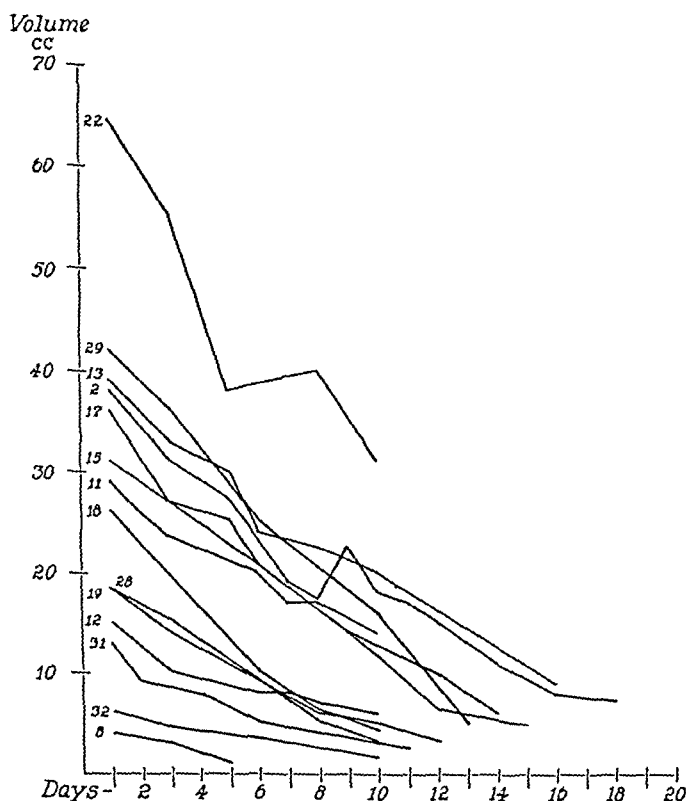


CHART 1—Actual curve of healing as measured in cubic centimeters in the 14 cases where the rate of repair was considered normal

RESULTS—Rate of Healing of Infected Wounds Precise measurements of either volume or surface area, or both, were carried out in 20 wounds of varied etiology. In many instances, studies were necessarily discontinued prior to complete healing because of the patient's discharge from the hospital, change in the type of dressing, or necessity for skin grafting. No cases have been included, however, which were not followed for a sufficient period of time to permit accurate observation of the course of healing. Topical agents used included dry gauze dressings, moist saline dressings, alcohol dressings, iodoform gauze, azochloramide 1:500 in triacetin, azochloramide in saline, merthiolate 1:1000, katadyn silver, Dakin's solution and zinc peroxide cream. Two cases received sulfanilamide by mouth. Aerobic and anaero-

bic cultures, together with bacterial counts by the method previously described, were made routinely

The rate of healing was considered entirely normal, within the limits of experimental error, in 14, or 70 per cent, of the 20 cases. Two of the remaining cases had a normal curve of healing after prolonged latent periods of from six to eight days. The rate of healing by granulation, as determined by volume measurements, assumed a regular geometric curve parallel to the expected curve of healing as calculated by DuNouy's¹² formula for the healing of superficial wounds. Chart 1 shows the actual curves of volume measurements in the 14 cases cited above, wherein the rate of repair was considered normal. In Chart 2, the actual size of a wound, as determined by both volume and surface area measurements, has been compared to the

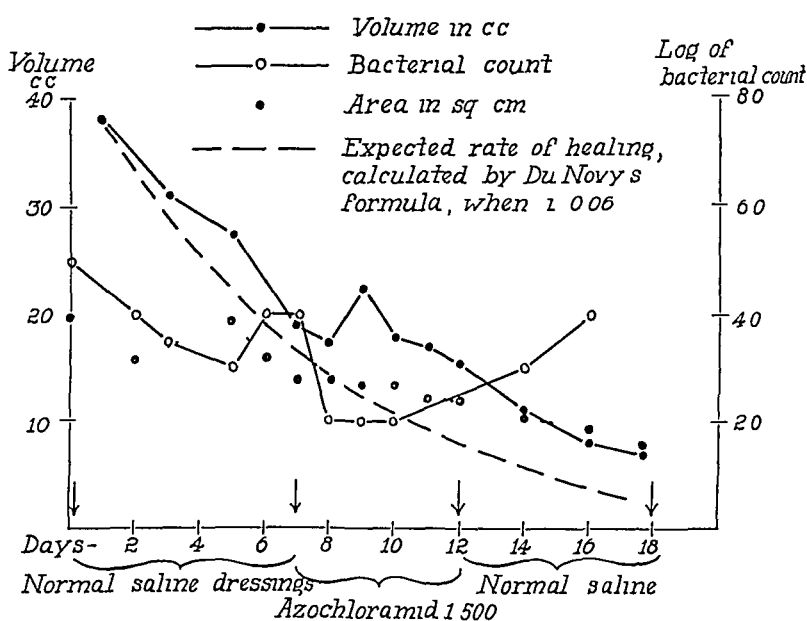


CHART 2—Case 2 Actual rate of healing in a wound of the thigh, as determined by both volume and surface area measurements compared with the expected curve of healing. The bacterial count was lowered with azochloramide dressings.

expected curve of healing. It is interesting to note the decrease in surface area of this granulating wound as compared to the volume changes. The early decrease in surface area occurred prior to actual epithelization and must be accounted for on the basis of contraction.³⁰ It seems likely, that the sharp vertical slope of the volume curve at the onset of healing may be due almost entirely to contraction, the actual rate of granulation remaining constant throughout the period of healing.

Wide variations in the degree and type of infection occurred in the 14 cases showing normal healing curves. As stated previously, all of the wounds were grossly infected, though adequately drained and without extensively undermined recesses. A review of the brief case summaries appended, will reveal that the causative organisms included the common bacteria found in surgical wounds. A few of the antiseptic agents, notably azochlor-

ANTISEPTICS AND WOUND HEALING

mide and iodoform packing, showed a definite tendency to lower the bacterial count in granulating wounds, and in such cases the clinical appearance of the wound was improved in that there was less exudate and less odor. The decreased number of bacteria and the improved clinical appearance of the wound apparently resulting from the local application did not, however, tend to stimulate healing. At the same time no deleterious effect on the rate of healing could be attributed to any of the agents employed locally. Wounds in this group healed at a constant, regular rate, irrespective of the bacterial flora or the topical agent used in the dressing.

Six of the 20 wounds in this series failed to heal at a normal, regular

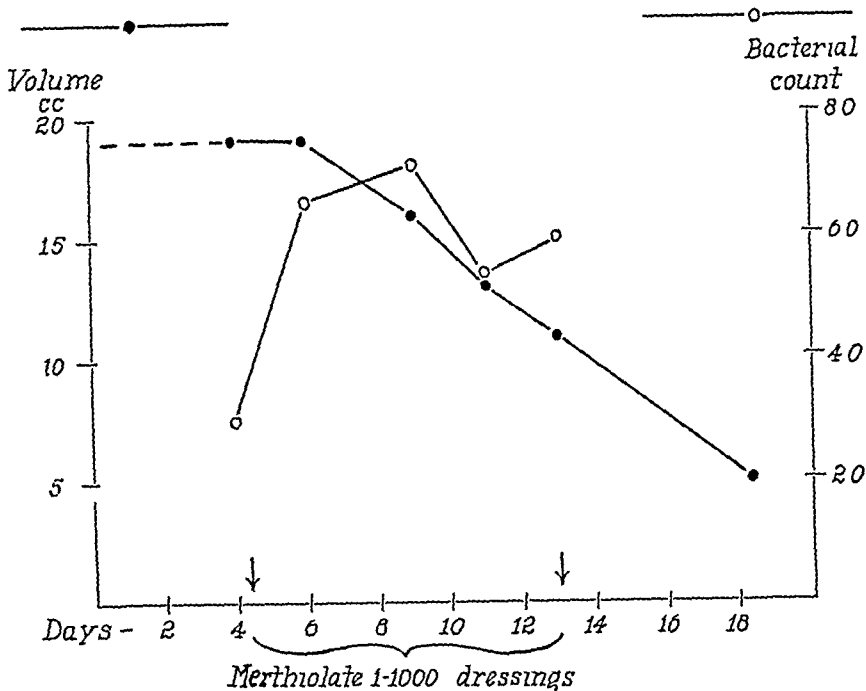


CHART 3—Case 30 Prolonged latent period, apparently due to necrotic fascia at the base of the wound. The bacterial count increased, notwithstanding the application of 1:1,000 merthiolate dressings.

rate. Particular attention was directed toward the study of these cases for remote causes of delayed healing, but in only one instance was such a cause discovered. A latent period of six to eight days occurred in Case 9, a female, age 60, with moderately severe diabetes. In the remaining five cases the delayed healing must be attributed, insofar as can be determined, to local causes. The two wounds studied in Case 1 presented a clinical picture and bacteriological findings similar to the type of chronic progressive undermining ulceration, which has been described by Meleney^{31, 32} as due to the micro-aerophilic, hemolytic *Streptococcus*. The progressive lesion, and failure of normal healing in such cases is due to a specific, locally invasive type of infection with continuing tissue destruction. Normal rate of wound healing in this case did not occur until a radical excision and treatment with zinc peroxide had been instituted.

The three remaining wounds in the group, where repair was retarded, varied in etiology, location and bacterial flora. The presence of devitalized,

necrotic fascia, affording a foothold for invasive organisms, was a factor common to all of these wounds, which undoubtedly delayed wound repair. The wound in Case 30 (Chart 3) was relatively clean, being only mildly infected with nonhemolytic *Staphylococcus aureus*. A latent period of 8 days was observed in this wound, during which time necrotic fascia at the base of the wound remained exposed and granulation did not progress. Normal granulation occurred after the fascial slough had completely sep-

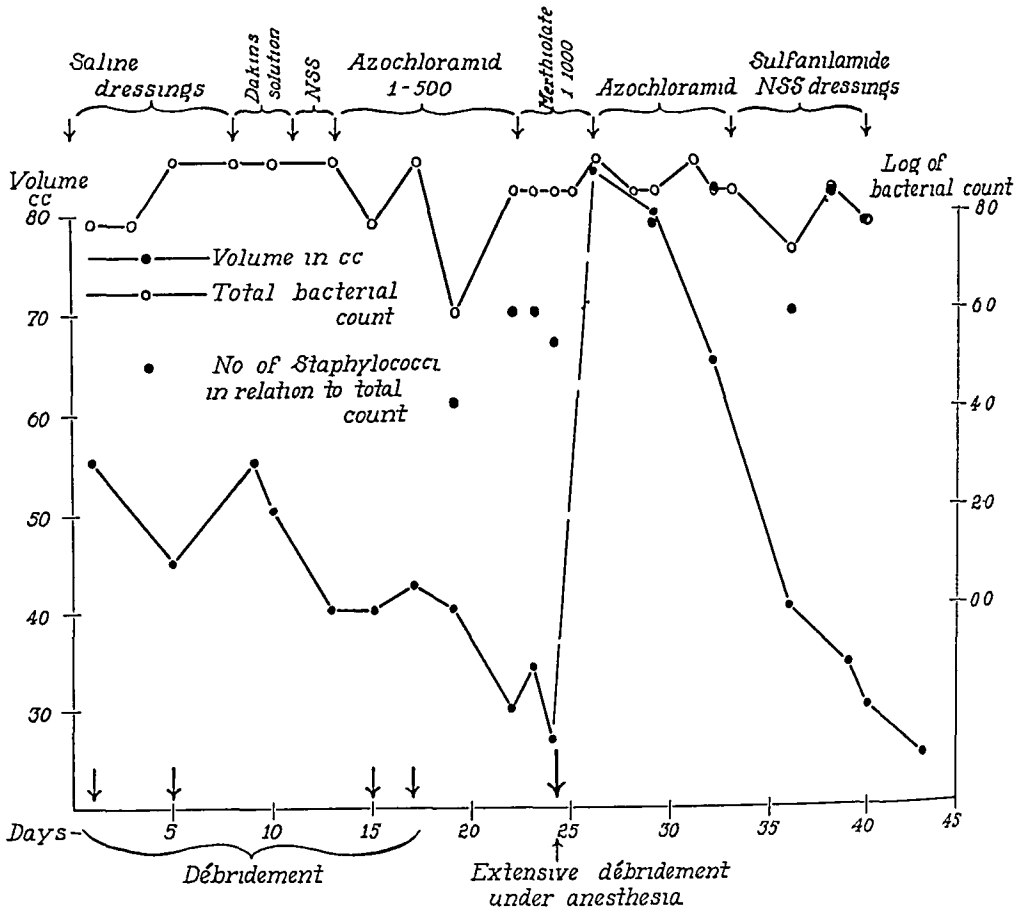


CHART 4—Case 25 Retardation of wound healing, due to fascia necrosis with persistent infection. The bacterial count was not influenced by antiseptics.

arated, although an actual increase in the bacterial count took place. A similar course of events occurred in Case 14, a wound grossly infected with hemolytic *Bacillus coli*. The complete curve of healing of the third wound, Case 25 (Chart 4), demonstrated a retardation of healing during the period of fascia and muscle necrosis in a wound infected with *Streptococcus hemolyticus* and *Staphylococcus aureus*. The rate of repair in each of these three cases approached the normal expected curve of healing only after mechanical débridement or natural sequestration of devitalized tissues. The subsequent course of healing, then, did not differ from that observed in the cases cited above in which there was no excessive tissue necrosis and no retardation of repair.

The Effect of Topical Agents on the Healing of Infected Wounds
Studies of the effect of topical agents on the bacterial flora were conducted in a total of 23 cases. The technic employed has been previously described. Complete studies of the rate of healing were conducted in 20 of these cases.

The agents used locally may be divided into two groups: (1) Admittedly inert materials—dry gauze and moist saline dressings; (2) Antiseptic agents—azochloramide 1:500 in triacetin, azochloramide in saline, 70 per cent alcohol, merthiolate 1:1000 aqueous solution, Dakin's solution, katadyn silver,

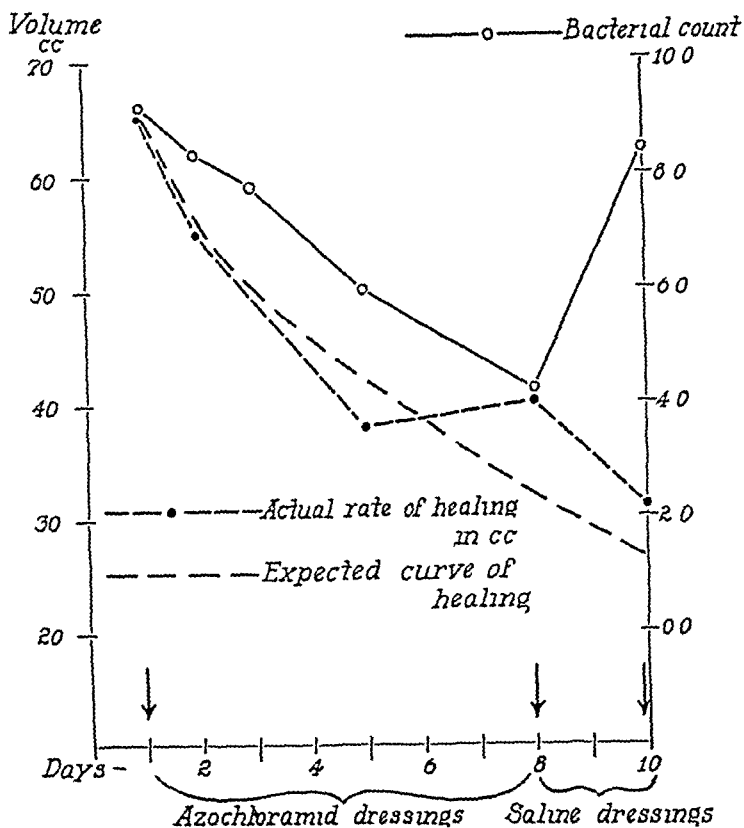


CHART 5—Case 22. Favorable influence of azochloramide on surface infection of a normally granulating wound.

2 per cent acetic acid and zinc peroxide cream. In two cases sulfanilamide was administered by mouth.

In the group of granulating wounds which were free of necrotic tissue, azochloramide and iodoform gauze did influence the bacterial counts. Charts 2 and 5 show representative curves of the logarithm of the bacterial count in such cases. The diminution in the number of organisms, however, was not associated with rate of wound healing above the expected normal. In wounds containing sloughing tissue, no appreciable change in the bacterial content was observed with the use of any topical agent (Charts 3, 4 and 6). Clinical improvement and a normal rate of healing were observed after the use of extensive debridement and zinc peroxide cream in two chronic burrowing ulcers. Quantitative bacterial counts were not attempted during the period when zinc peroxide was employed, because of technical difficulties, so that the exact effect of this agent on the degree of infection cannot be

definitely determined Two per cent acetic acid, applied at frequent intervals, lowered the bacterial count of *Bacillus pyocyaneus* in two cases under observation, although the total bacterial count remained unaltered, because of the presence of a mixed infection with *Staphylococcus aureus*

With the above exceptions, no topical agent had any appreciable effect on the bacterial flora of the wounds in this series It may further be stated that, with the exception of zinc peroxide in infections where it is specifically indicated, none of the agents studied had any beneficial action on wound healing The few antiseptics which influenced the bacterial counts in relatively healthy granulating wounds had no effect in the presence of tissue necrosis, which seemed to be constantly present whenever a wound increased in size or failed to heal because of a local factor We think it advisable,

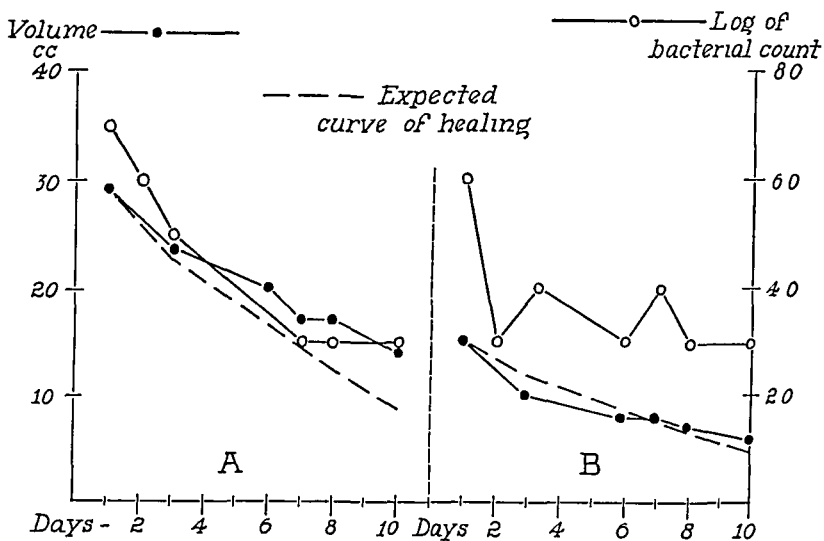


CHART 6—Case 11 Bilateral infected wounds. Wound A was treated with normal saline and Wound B, with azochloramide for the first six days, with no appreciable difference in the bacterial counts of the two wounds

however, to call attention to the action of one of the agents in this group, namely, Dakin's solution, which was used at two to three hour intervals for three days in one case without appreciable influence on the bacterial count (Chart 4) The action of Dakin's solution on necrotic tissue,³³ affords a means of chemical debridement of a wound which is not possessed by the more stable chlorine antiseptics It seems to me that this action, peculiar to Dakin's solution, may account for the fact that it is outstanding as a local agent which has survived the test of adequate clinical trial for over 20 years Is it not possible that Dakin's solution shortens the healing period of dirty, sloughing wounds by hastening the separation of necrotic tissue, and not by any direct antiseptic action? Further speculation, based upon the critical study of this series of cases, and impressions gathered from other cases which were not suitable for quantitative study, persuades us that other specific local agents, notably zinc peroxide, which have received favorable clinical trial, may exert their action by creating an unfavorable environ-

ment for bacterial multiplication, rather than by any wholesale destruction of the offending organisms

It is not our purpose to consider the action of general agents on wound healing, but the use of sulfanilamide in two wounds infected with *Streptococcus hemolyticus* afforded an interesting observation which warrants mention. The drug was administered by mouth at six hour intervals throughout the 24 hours to two patients, similar total doses being used in each case. In Case 28, a pure culture of hemolytic *Streptococcus* was obtained at the time of drainage of an abscess of the thigh. Sulfanilamide therapy was started within a short time of operation. A culture, taken 36 hours after the treatment, was started and all subsequent cultures, aerobically and anaerobically, were negative for *Streptococci*, although a secondary invader was cultured. In Case 25, sulfanilamide therapy was employed five weeks after the drainage of an abscess of the lower leg, at a time when the wound contained necrotic tissue and was grossly infected with *Streptococcus hemolyticus* and *Staphylococcus aureus*. The sulfanilamide had no appreciable effect on the *Streptococci* in this wound, either because the organisms, lodged in dead tissues, could not be reached by the sulfanilamide present in the tissue fluid, or because the presence of necrotic tissue interferes with the action of sulfanilamide on *Streptococci*.³⁴

SUMMARY OF CASE REPORTS

Case 1—J C, age 47. Small ulcer over the inner aspect, left lower leg, with blebs over the external malleolus. Treated for three weeks with hot dressings, sulfanilamide, roentgenotherapy and gelatin boots over alternate periods without improvement. Edges of the ulcer curled, irregular and undermined with "daughter ulcerations" beyond the periphery. The ulcer was painful and tender to touch.

Culture Hemolytic *Streptococcus* and *Bacillus coli*

The ulceration continued to spread, in spite of the treatment noted above. Excision and treatment with zinc peroxide was followed by improvement though normal healing, as determined by skin area measurements, did not occur until five days after a second, more extensive excision of the undermined skin edges. Successful pinch grafts were obtained two weeks after radical excision and zinc peroxide treatment.

A similar, though smaller, chronic, progressive ulceration of the right lower leg was followed with skin surface area measurements for one week, without showing any tendency to heal. Radical debridement, zinc peroxide dressings and skin graft afforded an effective means of initiating healing.

This patient's general health and nutritional status were good. Blood sugar was normal and Wassermann was negative.

Case 2—A S, age 13. Granulating wound of the left thigh extending down to the fascia lata, following surgical incision and drainage of a subcutaneous abscess.

Culture Hemolytic *Staphylococcus aureus*

Dressings were started six days after operation, at the time of removal of an iodoform pack which was placed in the incision at operation. Normal saline and azochloramide 1:500 in triacetin, were used locally over alternate periods.

Case 8—J McC, white, male, age 34. Infected herniorrhaphy wound. Lower angle of the incision opened down to the external oblique fascia and measurements started 24 hours later.

Culture *Staphylococcus aureus*

Moist normal saline dressings Healing was normal, and the latent period of less than 24 hours' duration

Case 9—H C, colored, female, age 60 Surgically clean wound of the back following excision of a small carbuncle

Culture Staphylococcus aureus

Patient was a severe diabetic, controlled by diet and insulin Nutritional status and general health were otherwise good The latent period was six to eight days' duration, with normal healing curve thereafter

Case 11—L P, white, male, age 66 Bilateral wounds of the buttocks following surgical incision and drainage of localized abscesses, resulting from the intramuscular injection of medication

Culture Staphylococcus aureus obtained from both wounds

Dressings started 24 hours after incision and drainage Alternate dressings of normal saline and azochloramide 1 500 in triacetin Normal healing occurred, with no demonstrable latent period

Case 13—T K, white, male, age 37 A wound of the back following surgical excision of a large carbuncle Measurements started six days after the operation, at which time the edges of the wound were necrotic and sloughing and there was an area of necrosis at the base The wound was superficial to the fascia

Culture Staphylococcus aureus

Dressings of normal saline packs and azochloramide 1 500 in triacetin, over alternate periods, changed at 48-hour intervals Normal healing occurred

Case 14—E F, white, male, age 60 to 70 Infected incision following appendectomy, with drainage Incision opened widely, two weeks after operation, because of infection and undermining, and measurements were started at that time Slough and necrosis involved the fascia of the external oblique

Culture Bacillus coli and diphtheroids The culture was repeated three times during the course of study

Dressings of normal saline and merthiolate were employed over alternate periods Nutritional status and general health were good except for mild anemia Red blood cells, 3,900,000 Blood sugar and urea, normal Kahn, negative Serum proteins, normal Delayed healing was noted by volume measurements and infection was not controlled by the antiseptic dressings

Case 15—L O'K, white, female, age 14 An incision of the left lower leg following surgical removal of the lower one-third of the left fibula for chronic, recurrent osteomyelitis, localized to the fibula

Culture Staphylococcus aureus

Measurements were started one week after operation, at which time the iodoform packing was removed Dry dressings, azochloramide 1 500, and merthiolate were employed over alternate periods General condition was good except for anemia (red blood cells, 2,000,000 to 3,200,000 during the course of the study), which was treated by transfusion prior to onset of the study Wound healing was normal

Case 17—M P, white, male, age 46 A wound over the lower right thoracic cage anteriorly, following resection of the ninth and tenth costochondral junctions for osteomyelitis, resulting from a previous transpleural drainage of an amebic liver abscess Dressings started four days after operation Merthiolate, azochloramide and normal saline were employed over alternate periods Normal wound healing resulted

Case 18—P W, colored, male, age 49 A wound resulting from incision and drainage of a localized abscess about a silk suture, in the external oblique fascia The abscess drained two months after the original operation, a herniorrhaphy There was marked inflammatory edema and local phlebitis of the tissue surrounding the abscess Roentgenotherapy of 100 R was used four times prior to the incision and drainage The patient's general condition was good

Culture Staphylococcus albus and aureus

Dry dressings and katadyn silver were used Normal healing occurred

Case 19—H B, colored, male, age 38 Localized abscess of the buttock in which dressings were started three days after incision and drainage

Culture Bacillus proteus and hemolytic Staphylococcus aureus

Dressings of katadyn silver and azochloramide during alternate periods General condition of the patient was good except for empyema thoracis, adequately drained Wound healing was normal

Case 22—J T, white, male, age 32 An infected right lower rectus surgical incision following exploratory celiotomy Measurements started 36 hours after the incision was opened

Culture Staphylococcus albus and aureus

Dressings of normal saline, azochloramide and 70 per cent alcohol were employed Healing was normal

Case 25—W S, white, male, age 54 A cellulitis of the right lower leg, secondary to infection of the great toe, with extensive muscle and fascia necrosis at the time of operation Further debridement performed one week following original incision and drainage Study was started at this time General health was good

Culture Streptococcus hemolyticus and later secondary infection with Staphylococcus aureus

Dry dressings, Dakin's solution, azochloramide, merthiolate and sulfanilamide were employed Normal healing did not begin until 29 days after the beginning of the study

Case 28—J S, white, male, age 60 A superficial abscess in the anterior surface of the thigh, secondary to a streptococcic infection of the toe

Culture Streptococcus hemolyticus

Dry dressings and sulfanilamide per ora were used Normal wound healing resulted

Case 29—M S, white, female, age 50 A wound of the back following surgical excision of a cutaneous neoplasm General condition was good

Culture Bacillus proteus and Staphylococcus aureus

Dressings consisted of iodoform packing changed every 48 hours, and dry gauze packing Normal wound healing resulted

Case 30—A G, white, male, age 44 A right subcostal incision for a cholecystectomy, with disruption of the wound down to, but not including the fascia, though the fascia was exposed and was necrotic, the wound was surgically clean

Culture Staphylococcus aureus

Dressings of merthiolate 1:1000 were employed throughout the study There was a latent period of six to seven days, after which healing progressed at a normal rate

Case 31—M Q, white, male, age 62 A decubitus ulcer of the sacrum, extending down to the muscles, on which dressings and measurements were started 24 hours after debridement and excision Iodoform gauze dressings were employed The wound repair was normal

Culture Staphylococcus aureus and Bacillus proteus

Case 32—F V, white, male, age 51 A decubitus ulcer over the lower back, which was thoroughly debrided Normal healing occurred

Culture Staphylococcus aureus

SUMMARY AND CONCLUSIONS

It is apparent from the above observations that the majority of infected wounds, adequately drained and not containing sloughing tissue, in normal individuals, will heal according to a regular geometric curve, the rate being proportional to the size of the wound and decreasing with the age of the patient, regardless of the type of local treatment Infection with invasive organisms in the presence of extensive necrosis and the presence of dead

tissue in the wound, even without active infection, are the outstanding local causes of retarded healing. This is in accord with the statement by Arey⁵ that "In open wounds, which are healing by granulation, the formation of fibrils depends on the prevailing metabolic conditions. While the destructive phase is still in progress, fibrils are not formed. In a similar manner regions of necrosis or areas containing foreign bodies and rich in bacteria have an abundance of cells and are thus not favorable to fibril development. Only when all dead and foreign material is removed, either by enzymic digestion, phagocytosis or sloughing, does fibril formation progress."

The group of local agents considered in this study had little, or no, beneficial effect upon the healing of infected wounds, except for the action of zinc peroxide in specific cases. The few antiseptic agents which had definite bactericidal action on surface organisms in normal granulating wounds were ineffective in the presence of tissue necrosis, and it is only under the latter circumstances that the existing infection is likely to retard healing.

(1) Healing of granulating wounds under normal conditions, as determined by precise volume measurements, occurs according to a regular geometric curve which may be expressed, in function of area and time, by the mathematic equation presented by Carrel and DuNouy for the normal cicatrization of clean surface wounds.

(2) The presence of a large number of organisms on the surface of wounds does not ordinarily retard healing. Specific types of infection with invasive organisms, and the presence of necrotic tissues and inadequately drained areas of infection, are the outstanding local causes of delayed repair.

(3) A quantitative study has been made of the effect of local agents, particularly antiseptic substances, on the rate of healing and the bacterial flora of infected wounds. The following conclusions may be formed on the basis of this objective investigation of a limited number of commonly used vulneraries:

(A) Topical agents will not prevent further tissue destruction and retardation of repair in the presence of infection with virulent, invasive organisms by any direct antiseptic action. The few antiseptics, which decreased the number of surface organisms in wounds healing at a normal rate, were ineffective in the presence of tissue necrosis, and exerted no beneficial effect on the rate of wound repair.

(B) No evidence was obtained to indicate that any of the agents in this series retarded healing by excessive chemical irritation of tissue cells. There is, then, no apparent contraindication to the use of antiseptic dressings in the prevention of infection in surgical wounds.

In the management of infected wounds, less attention should be given to the selection of a potent local antiseptic agent. It is of more importance to consider the problem of increasing local tissue immunity, which may be influenced by factors of a general nature remote from the site of the wound, and aiding the sequestration of necrotic tissues rich in bacteria by mechanical or chemical debridement and adequate surgical drainage.

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THE EFFECT OF URINARY BLADDER TRANSPLANTS AND EXTRACTS ON THE FORMATION OF BONE

A FURTHER EXPERIMENTAL STUDY

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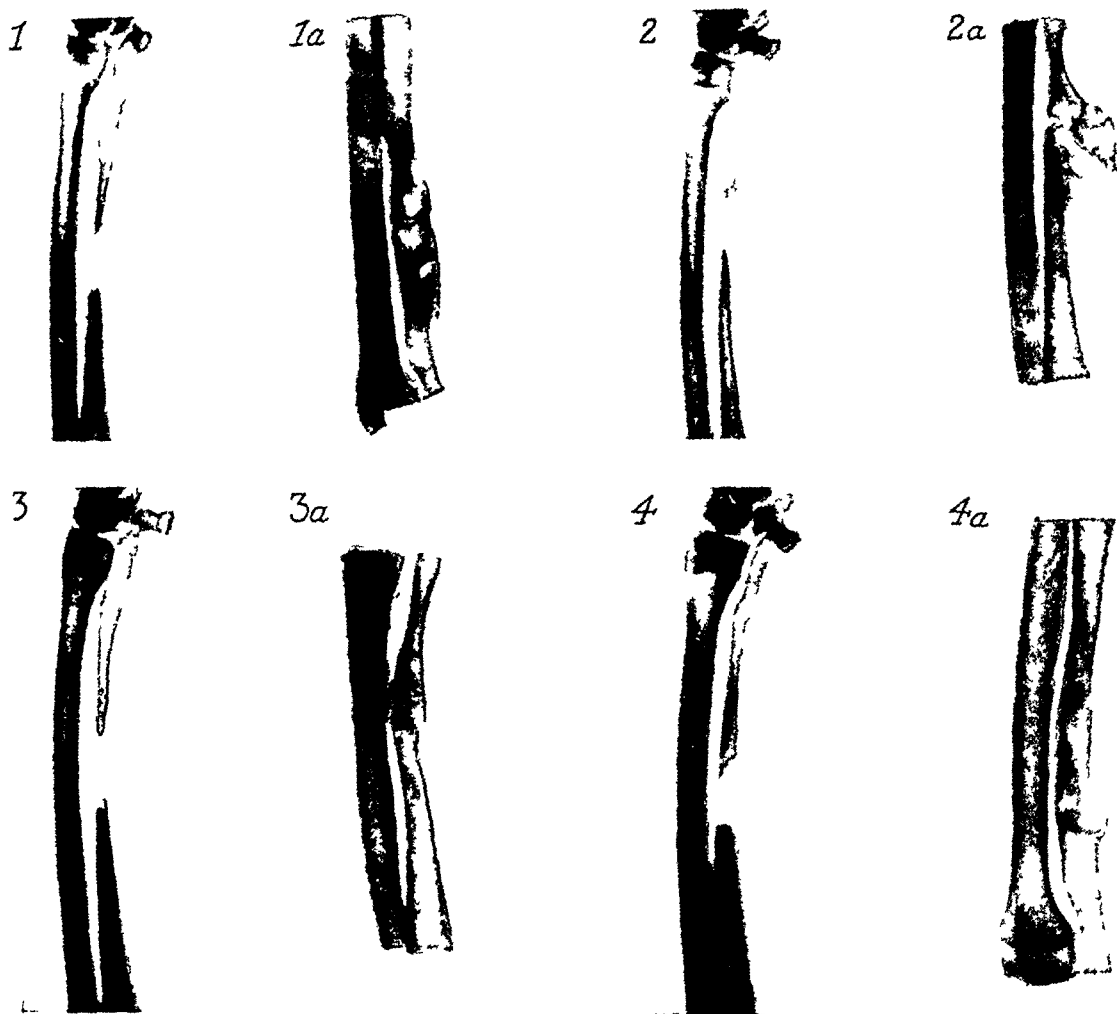
THE remarkable influences of urinary bladder transplants on the healing of defects of bone and on hyaline cartilage have been reported¹ These studies were based on the observation of Huggins,² who found that the epithelium of the urinary tract of the dog after autotransplantation is capable of inducing ossification in certain connective tissues We confirmed this observation that the newly formed bone bears an intimate relationship to the proliferating bladder epithelium and is true membranous bone with haversian canals and hematopoietic bone marrow Our results in other experiments indicated that the presence of a growing transplant of epithelium from the urinary bladder of the dog stimulates osteogenesis and tends to cause union in defects in long bones which would ordinarily result in nonunion In the latter experiments, defects were made in the ulnae of dogs by subperiosteal removal of a section of the shaft At the same operation the defect in the ulna on one side was bridged by an autogenous transplant of epithelium obtained from the urinary bladder The defect in the opposite ulna was kept as a control, and nonunion resulted in 14 of 16 controls in which the experiments lasted from one to nine months Bone was formed in the defect containing the growing epithelium of bladder, and this formation of new bone resulted in union

The size of our experimental defects in ulnae were probably adequate, and the evidence indicated that the new bone was formed directly under the influence of the growing bladder epithelium and was not the result of formation of bone from the periosteum bridging the defect However, it seemed desirable to perform other experiments in which the defect was created in the bone at one operation and, after the occurrence of nonunion had unquestionably been established several months later, make the transplantation of epithelium at a second operation The influence of the periosteum over the defect alone, and in association with bladder epithelium, was noted by this method and, also, by performing some operations in which all of the periosteum, including that along the interosseous membrane, was removed along with a long section of bone The results obtained from these two experimental methods are herewith reported A review of the literature on heteroplastic formation of bone has been made by Huggins

Experimental Methods—With the dog under ether anesthesia and using aseptic technic, the shaft of the ulna of each leg was exposed and 2 to 5 cm

BLADDER TRANSPLANTS ON BONE

of the bone was resected subperiosteally in equal amounts on each side. The wounds in the two legs were then closed. This operative procedure was performed in six adult dogs, one of which died during the period of observation. After a lapse of time varying from 14 to 16 weeks, roentgenograms were made of the legs of the five dogs. None of the roentgenograms showed any evidence of new bone bridging the defects in either leg. In addition to nonunion, the ends of the bones at the site of the defects were found to have



FIGS. 1, 2, 3 and 4—Roentgenograms showing defects in the right and left ulnae of two dogs, which had been created 14 weeks previously. The periosteum was not removed with the bone.

FIGS. 1a, 2a, 3a, and 4a—Roentgenograms made of the corresponding legs, 15 weeks after the defects in the ulnae had been bridged by autogenous transplants of bladder mucosa. The defects are filled by a mass of bone which contains numerous cysts. Firm union is present with the exception of that evidenced in 2a.

undergone rarefaction and had decreased in diameter. At this time, 14 to 17 weeks after creating the defects of the ulnae, the dogs were operated upon again. The healed operative wounds of the legs were opened and a condition of nonunion of bone found. The ends of the ulnae, at the site of the defect, were denuded slightly with rongeurs and a bed made in the scar tissue and periosteum for a transplant. The urinary bladder was exposed and a piece of the entire wall of the dome of the bladder was excised. The defect in the bladder and the abdominal incision were then sutured. The mucous membrane of the piece of excised bladder was then dissected from the muscularis

and was divided into two equal portions. One of these portions of mucous membrane was sutured into the defect of each ulna. The transplant was stretched from one end of the defect to the other end and was held in place by silk sutures. The wounds in the two legs were then closed in layers. The dogs were sacrificed 15 weeks later. The front legs were examined grossly, by roentgenograms, and microscopically. Specimens of blood were taken from the dogs prior to making a transplant, approximately a week after-



FIGS 5, 6, 7 and 8—Roentgenograms showing defects in the right and left ulnae of two dogs, which had been created 36 weeks previously. The periosteum was removed with the corresponding portion of bone. Note that the lengthy and old defects are associated with marked atrophy of the ends of the bone.

FIGS 5a and 6a—Roentgenograms of the corresponding legs, 108 weeks after the defects in the ulnae had been bridged by autogenous transplants of bladder mucosa.

FIGS 7a and 8a—Roentgenograms of the corresponding legs, 60 weeks after transplantation of bladder mucosa into the defects.

The marked increase of the amount of bone in Figures 1a, 2a, 3a and 4a, where the periosteum was not resected with the bone over Figures 5a, 6a, 7a and 8a where the periosteum was removed with the bone, is evident. Union was much more firm, in the experiments where the periosteum was not removed.

wards, and just prior to autopsy, for determinations of the serum calcium and phosphorus.

Exactly the same operative procedures as have been described were carried out on another group of six dogs, except that when the defects were created in the ulnae the corresponding portions of periosteum were removed entirely. This group differed from the first group of dogs also, in that nine months were allowed to elapse between the time of the resection of the bone and periosteum and the transplantation of mucous membrane into the defect, and in that the dogs were permitted to live 27 months after the transplantation before being sacrificed. Two of the dogs died during the course of the experiments. One of these deaths, occurring one year after operation for transplantation, was caused from a gangrenous urinary bladder and pyelonephritis produced by a huge bladder stone. The changes in the defects were followed by occasional roentgenograms.

Results—Gross Examination—New bone was formed in ten of the 12 defects made in the first group of six dogs where the periosteum was not removed from the bone. The production of bone was marked and union occurred in nine out of ten defects that were bridged by new bone. The mass of new bone contained multiple cysts of various sizes similar to those that have been described. The cysts possessed epithelial lined walls and contained a brownish fluid.

Roentgenologic Examination—Roentgenograms made at the conclusion of the experiments, 15 weeks after making the transplants, showed, with the two exceptions mentioned, that the defect was occupied by a mass of dense bone and some clear areas. The latter represent multiple cysts. The ends of the bone near the defect were no longer atrophic.

Microscopic Examination—The defects were filled with an adult type of bone and with many cysts and masses of bladder epithelium. The cysts were lined with bladder epithelium. In general, the cysts were not so large as those found in shorter experiments. As has been noted previously, all of the newly formed bone in the defect was not immediately adjacent to bladder epithelium. Much of the new bone, however, was laid down beside the cyst walls with only a thin layer of tissue intervening. The new bone contained haversian canals and adult bone marrow. The ends of the fragments of bone at the site of the former defect were of normal appearance.

Determinations of Blood Calcium and Phosphorus * Analyses were made of the blood serum of this latter group of dogs just before transplantation of the bladder mucous membrane, and seven and 111 days afterwards, and, as shown in Table I, there were no significant changes in the serum calcium and phosphorus.

Interesting results were obtained in the long term experiments with the second group of dogs, in which there was removed with the segment of bone all of the corresponding periosteum. Four of the six dogs lived until the completion of the experiment.

* These studies were made in the laboratory of Dr. Alexis Hartmann.

TABLE I

DETERMINATIONS OF BLOOD CALCIUM AND PHOSPHORUS, PREOPERATIVE, AND SEVEN AND 111 DAYS POSTOPERATIVE

Dog No	Mg of Serum Calcium			Mg of Serum Phosphorus		
	Before Transplant	Seven Days After	111 Days After	Before Transplant	Seven Days After	111 Days After
12	11 3	12 9	12 0	5 0	3 4	3 3
318	12 0	12 9	12 3	3 4	3 7	4 5
B2	12 0	11 8	13 5	5 6	5 1	3 8
A18	11 9	11 7	12 3	3 6	3 1	3 8
354	11 6	12 0	12 5	5 7	5 5	6 2

The defects in five of the eight ulnae were completely bridged by a tubular mass of calcified tissue containing bone cysts. Four of the defects were only partially filled. The union of the ends of the bone was firm but not solid in the specimens where the defects were entirely bridged with calcified tissue.

Roentgenologic examinations were made of the defects nine months after they were created and prior to transplantation of bladder epithelium. These films revealed long defects in the ulnae in which there was no evidence of regeneration of bone. Atrophy of the ends of the bone was indicated by their marked decrease in diameter and by rarefaction. Roentgenograms were made at intervals during the experiments and, finally, they were made at the time of the conclusion of the experiments, 15, 18 and 27 months after transplants of bladder epithelium were made to the defects in the bones. The roentgenograms revealed the ends of the bones to be connected in five of the eight specimens by a tubular-like calcified mass containing some clear spaces known to represent cysts. The defects in the other three specimens were bridged only in part. The ends of the bone had increased in diameter and in density. The new bone in general was not so dense as the old, and while it was irregular in circumference it tended to resemble cortical bone.

Microscopic Examination—Cross-sections of the bone bridging the defects show a cyst lined by bladder epithelium surrounded completely by a ring of bone except for a sector comprising about one-eighth of the circumference. Other cysts of various sizes are adjacent. The cyst contained the remains of a granular material that failed to stain and that probably filled the cyst when it was viable. The large cyst was lined by a thin layer of atrophic bladder epithelium having occasional papillary projections into the cyst. Immediately adjacent to the thin basement layer lies a circular mass of adult bone containing numerous small cysts lined by bladder epithelium, haversian canals and small amounts of hematopoietic marrow. The bone is being formed from dense connective tissue by a process that has been described in a preceding report.¹ The connective tissue was formed between bundles of muscle fibers, after the resection of the bone and periosteum to create the experimental defect. There is no evidence that periosteum took part in the formation of the bone, and cartilage was not seen in the sections.

*Experiments, Employing Extracts of Pig's Bladder*¹—In view of the striking ability of transplanted bladder epithelium, in all of our experiments, to produce calcification, we have made further attempts to isolate from this epithelium a substance capable of reproducing the same phenomena. This is an extension of previous experiments made to secure a potent extract from urinary bladder epithelium.¹

Extractions of pig's bladders were made with water at a p_{H_2} . The extract was filtered at a p_{H_2} and salted out with sodium chloride. The aqueous extracts were adjusted to p_H 's of 2, 5, and 7.5, 0.2 per cent phenol was added as a preservative. The extracts were filtered through paper and then passed through a Berkfeld filter. The total solids of the extracts varied from 2.25 to 7.78 per cent.

Alcoholic extractions were made similarly with 60 per cent alcohol. Other extracts were made without the salting-out process in order to eliminate NaCl which might influence the results. These extracts were made by filtering and by dialyzing against tap water. A control extract was made from fresh pig's heart.

All bladder extracts were made from fresh, whole pig's bladder, as it was found impractical to remove the mucosal lining.

The intravenous injections of various dosages of these extracts did not produce any notable effects on the blood calcium and phosphorus of dogs that were attributable to the extracts directly. The frequent and continued hypodermic injections of the extracts about and into the fascia of the abdomen resulted in formation of inflammatory tissue at times, but bone was not produced in any instance. Acceleration of the union of bone was not produced by local injections of the extracts into experimental defects and fractures.

A diurnal variation in the (inorganic) serum calcium was found while making several consecutive, daily quantitative determinations of blood calcium on many normal fasting dogs for control studies. During the morning there was found consistently a rise of one to two milligrams of calcium. After reaching the peak of the rise about noon, there was a slow return of the serum calcium to normal. We have not found a reference to this observation on dogs. The phenomenon is not found in man.

COMMENT AND CONCLUSIONS

The results obtained from these experiments further amplify the fact that epithelium of the urinary bladder of the dog when transplanted has the ability of inducing ossification in certain connective tissues. The newly formed bone bears a constant and close relationship to the proliferating epithelium and as a result there is produced ossification of connective tissue through the medium of osteoblasts. This method of ossification has been used to unite the ends of a defect of long standing in the ulna of the dog.

¹ Supplied by the Lilly Research Laboratories. Chemical determinations made by Robert Breitenbach.

Firm union of the ends of the defects was usually produced by the osteogenic stimulus when the periosteum was not resected with the bone. When the periosteum was entirely removed with long sections of bone, it was possible to bridge the gap with true membranous bone, but firm union of the ends of the bone did not result. The newly formed bone in the defects assumed a tubular shape similar to that of normal bone and the ends of the bone were no longer atrophic under the influence of the bladder epithelium. The entire mechanism by which the proliferating bladder epithelium causes formation of bone is not known. Ossification of the defects was greatly aided by the presence of periosteum and was not preceded by the formation of cartilage. No theories are proposed to explain the mechanism of calcification. It is necessary that calcium salts be present locally in large enough quantities for utilization by osteoblasts. We have not been able to establish the action of an enzyme in the process of calcification, other than that phosphatase is known to be present in the region of ossification in a fairly high concentration. Doubtless the formation of bone under our experimental conditions will be found to be regulated by a complexity of interrelated factors acting in coordination similar to those concerned with the calcification of the normal skeleton.

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THE APPARENT ALTERATION OF TETANUS TOXIN WITHIN THE SPINAL CORD OF DOGS[†]

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IN 1935 and 1937, a series of experiments was carried out which showed that pure reflex motor tetanus (clonic spasms) can be produced without the accompaniment of the slightest degree of muscular rigidity. To demonstrate the separation of these two cardinal manifestations of tetanus, it is necessary to inject only minute quantities of tetanus toxin into an anterior horn of the dog's spinal cord. Previously Abel¹ and his coworkers had succeeded in bringing about a state of unyielding rigidity in the limbs of dogs by multiple intramuscular injections of tetanus toxin. They have shown that by the deposition of 1/8,000 of the ordinary lethal dose of this toxin at each of 40 different sites one can render the hind limbs of a dog rigid for three months. This observation added weight to their contention that the cause of muscular rigidity, as seen in both local and general tetanus is to be found in the action of the toxin on the voluntary muscles, and not in its action on any part of the central nervous system. To substantiate this belief we attempted the experiments referred to above. The demonstration that the effect of tetanus toxin on centers in an anterior horn of the spinal cord is the production of pure reflex motor tetanus was made in 11 dogs. The protocols of these experiments were the basis of an article which appeared in February, 1938.² The observations on these 11 dogs have been fully and accurately confirmed in 14 additional experiments. The present communication is not concerned with the confirmation of the preceding report, but deals with the study of an unexpected and unexplained phenomenon which occurred consistently. We refer to the observation noted in a preceding communication,² that every dog receiving an intraspinal injection of tetanus toxin died, although the quantity employed was a tiny fraction of the lethal dose given by any other route. In an effort to understand the cause of death following the intraspinal injection of tetanus toxin we have carried out a series of experiments that are herein reported. This study has led to the formulation of a new theory of the pathogeny of tetanus.

Before recording the actual experiments, however, it is necessary to describe the technic that has been devised for accurately depositing as little as 1/2,000 cc at any given site. It is also desirable to make some statements concerning the dosage and the materials used in the experiments.

In all of our experimental work we have used batches of tetanus toxin prepared by Dr. Bettylee Hampil of the Sharp and Dohme laboratories. The

[†] These researches were aided by a grant from the John and Mary Markle Foundation.

details of the method of preparation will be furnished upon request. The toxin has been kept in sterile rubber-stoppered vials at 2° to 4° C. Not only has Doctor Hampil run preliminary assays of each shipment of toxin, but Dr. William Chalian, working in Dr. John J. Abel's laboratory, has repeated these preliminary assays and from time to time has reassayed each vial to detect any loss in potency. Bacteriologic studies have been made to guarantee the continued sterility of the toxins. Various dilutions of toxin, Batch No. 678, were made by Dr. John Brewer in the Department of Bacteriology. The dilutions were made with beef infusion broth, and the resulting mixtures were placed in sealed glass vials under nitrogen.

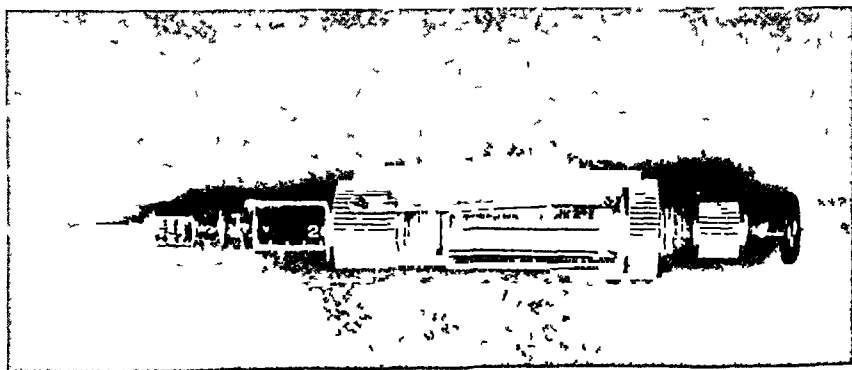


FIG. 1.—Photograph of syringe constructed in order to inject minute quantities of toxin.

Throughout our work we have adopted the dog unit described by Doctor Abel as follows: "We have found in the course of numerous experiments extending over a period of five years that injection of 480 guinea-pig LD 50's per kilogram invariably induces fatal tetanus in dogs of medium weight and age, and have arbitrarily chosen this figure as our lethal dose for dogs. This dose kills dogs taken at random in from five to nine days (when given intravenously, intramuscularly, or subcutaneously)." Neither a median nor a minimal lethal dose, but certainly larger than a statistically determined median lethal dose would be, it was adopted as a matter of convenience. We have always stated the dosage of the injected toxin in terms of standard guinea-pig units, so that our work can readily be checked by others without reference to our arbitrary dog unit."³

The technic for injecting minute quantities of toxin which was described in connection with our earlier spinal cord experiments was not infallible and was limited to a maximum of 0.003 cc. per injection, consequently, the apparatus illustrated in Figure 1 was devised and has been used in all animals whose number is over 104. This device† consists of a tuberculin syringe the barrel and plunger of which are held tightly by jackets of stainless steel. These jackets are threaded upon each other so that one complete turn either

* Parentheses ours.

† The authors wish to thank Dr. George Gey for his supervision of the design and construction of this instrument.

aspirates or expels 1/100 cc. Fractions of this amount are easily registered by the arm on the upper jacket which clicks at every tenth of a turn. It is entirely possible to turn the plunger accurately 1/20 of a turn, thereby delivering 1/2,000 cc. If a tuberculin syringe breaks, it is a simple matter to replace it. With this injection apparatus there may be an error of 0.0005 per 0.01 cc because of the variations in the bore of tuberculin syringes.

EXPERIMENT 1 *Method of Procedure*—This experiment was devised to ascertain whether or not the clonic spasms of the muscles which follow the injection of tetanus toxin into an anterior horn of a dog's spinal cord are responsible for the animal's death. To gain this knowledge a series of dogs was prepared in which toxin was placed in the distal end of the lumbar cord a few minutes after the conus and all adjacent spinal roots had been severed. By this procedure the usual evidences of reflex motor tetanus were eliminated. Postoperatively the animals had a flaccid paralysis of the hind limbs. From a study of Table I it is apparent that elimination of clonic spasms of the voluntary muscles does not prevent death following the intraspinal injection of minute quantities of tetanus toxin. Although the range of dosage given in Table I is from 1/12 to 1/50 of the ordinary lethal dose, these figures represent the maximum amount that could have been given. They do not allow for leakage and for loss of potency from exposure to the air. That this loss of potency can be as great as 50 per cent was accurately determined by assays.

Protocol of Typical Experiment—Dog No. 15, Male, mongrel, weight 8.3 Kg.

Operation in June 3, 1937. Under ether anesthesia, the operative field was shaved and prepared with a double application of iodine. The fifth, sixth, and seventh lumbar vertebrae were exposed and their dorsal spines and laminae removed. The operation was remarkable for the slight amount of bleeding. The conus and overlying dura were divided with scissors and the motor and sensory roots of the last three lumbar nerves on both sides were cut. The mobilized end of the cord with its surrounding dura was lifted from the spinal canal, and after all bleeding had been stopped by packing with moist gauze, a small opening was made in the ventral surface of the dura. A No. 25-gauge hypodermic needle was inserted into the central portion of the cord through this opening, and 0.003 cc of tetanus toxin, Batch No. 670, was injected. There was no obvious leakage upon withdrawal of the needle. The wound was closed in layers with silk. The amount of toxin injected represented at the most 1/50 of a lethal dose if given intravenously.

Following the operation the dog had a flaccid paralysis of the hind limbs. There were no clonic movements of any of the muscles. The dog died at 9:30 A.M. July 5, 1937. *Autopsy* showed a few intraperitoneal adhesions. The viscera were entirely normal. The wound was clean. Specimens were taken for microscopic study.

EXPERIMENT 2 *Method of Procedure*—The question arose whether or not injections of tetanus toxin into the white matter of the cord would be as lethal as those into the gray substance, accordingly, a group of dogs were given toxin in the region of one crossed pyramidal tract. All of the operations were performed in the lumbar region, the white fibrous band connecting the various denticulate ligaments served as a landmark for these injections. Following the laminectomy the dura was incised in the midline and the dural flap away from the operator was raised so as to expose a denticulate ligament.

This was cut to permit the cord to fall away from the dura and to facilitate rotation of the cord. Gentle upward traction on the dural flap served to bring the white line referred to above into clear view. The operator then inserted the tip of a No. 26-gauge hypodermic needle tangentially under this line. The depth of the puncture was easily controlled and in no instance was it more

TABLE I
CAUDAL PREPARATIONS

Date	Dog No	Toxin No	Dosage in Dog Units	Site of Injection	Symptoms and Remarks All the animals had flaccid paralysis of the hind limbs	Survival in Days	Autopsy
5/18/37	10	30A	1/12 or less	Anterior midline	No clonic spasms	5	Grossly normal
5/27/37	12	670	1/20 or less	Anterior right	Cord traumatized at operation	5	Hemorrhagic cystitis Otherwise normal
6/3/37	15	670	1/48 or less	Anterior midline	No spasms observed	2	Grossly normal Microscopic of cord
6/8/37	16	670	1/40 or less	Anterior right	No spasms observed	2	Bladder distended with bloody urine Slight consolidation in lungs
7/7/37	22	670	1/24 or less	Anterior right	No spasms observed	2	Grossly normal
7/7/37	23	670	1/33 or less	Anterior right	No spasms observed	1	Grossly normal
9/8/37	40	31A	1/50 or less	Anterior midline	Injectations not satisfactory Moderate hemorrhage from puncture wound	8	Grossly normal
9/18/37	42	31A	1/14 or less	Anterior midline	No spasms observed	2	Microscopic sections of cord Grossly normal

An additional animal was operated upon by a student assistant. The dog became emaciated and developed ulcers over both thighs, and died on the seventeenth day. It seems fair to assume that the injection was faulty.

CONTROLS

6/9/37	17	0	0	0	Operative control	30	Emaciation Considerable vomiting before death. Autopsy negative
9/20/37	45	31A boiled	1/13	Anterior midline	Foot injured and infected on eleventh P.O. day. Animal sacrificed on twelfth day	12+	Infected leg and thigh
9/21/37	48	31A boiled	1/14	Anterior midline	Developed ulcers on thighs from pressure necrosis	16	Infected ulcers Lungs consolidated
9/22/37	50	31A boiled	1/7	Anterior midline	Distemper	20	Massive consolidation of lungs Bloody fluid in peritoneal cavity
9/30/37	44	31A boiled	1/13	Anterior midline		5	Grossly normal

than 2 Mm. Frequently the point of the needle was so superficial that one could see a slight bulge following the deposition of the toxin solution. These injections were certainly made with greater accuracy than those aimed at the region of the anterior horn. This fact may account for the greater consistency in the results.

Eighteen animals were operated upon in this series. The amount of toxin injected ranged from 1/15 to 1/1,000 of an intravenous lethal dose. The eight dogs receiving smaller doses will be described in Experiment 6. In ten instances the dosage was approximately 1/20 of the calculated lethal dose. The physiologic alterations that ensued were the same in each of these ten animals. Death occurred with great regularity between 48 and 60 hours following the injection. No animal showed neurologic signs on the day of operation. The animals that were observed between 18 and 24 hours after the injection showed a little weakness in the right hind limb. Between 24 and 36 hours post-operatively, all of the animals showed hyperactive cutaneous and tendon reflexes in the right hind limb. In one instance gentle blowing on the foot pads would initiate a series of clonic contractions of the right hind limb but not of the left. Later all the animals showed constant muscular tremors or spontaneous clonic movements. These grew more severe until the animals were down. For a few hours before death the spasms were diminished. Not a single instance of rigidity (*Starre*) was observed, although in three dogs the contralateral limb was held in extension, nevertheless, in these three dogs the limbs were actively and passively flexed at all their joints. In two dogs there was a tendency to bite at the base of the tail as if the area annoyed the animal. There was not, however, any evidence of real tetanus dolorosus. One cannot draw any conclusion from this experiment because microscopic sections show that some of the toxin reached the anterior horn. The only advantage that white matter injections have over anterior horn injections lies in the greater accuracy with which the toxin can be placed.

EXPERIMENT 3 *Method of Procedure*—The possibility of the upward passage of tetanus toxin in the spinal cord was commented on in the earlier report on the experimental production of reflex motor tetanus. It was pointed out that after the introduction of tetanus toxin into the lumbar cord the resultant clonic spasms are strictly limited to the site of injection. This has been found true in all subsequent lumbar injections. Surely, if this exceedingly potent toxin passed *as such* to the medullary centers by way of the spinal cord, there would be some clinical manifestation en route. Furthermore, the absence of lymphatics in the cord lessens the possibility of such a passage. The amazingly rich network of blood capillaries makes it highly improbable that any readily absorbable molecule could migrate within a cord from the lumbar region to the medulla. In order, however, to prove beyond doubt that the molecule of tetanus never reaches the vital medullary centers by moving upward in the cord, we carried out a series of experiments with transected cords, the results of which are summarized in Table II. From a study of the data assembled in this table it is clear that the introduction of

TABLE II

TOXIN INJECTED INTO DISTAL SEGMENT OF TRANSECTED CORD

Dog No	Date of Transection	Site of Transection	Interval between Transection and Injection in Hours	Toxin No	Dosage in Dog Units	Site of Injection	Survival Period in Days	Autopsy
33	8/ 2/37	Dorsal 7	3/4	LYO-2	1/5-	Lumbar 4— right ante- rior horn	7	Infection of lower incision extend- ing down to cord
34	8/ 5/37	Dorsal 8	3/4	LYO 2	1/3-?	Lumbar 4— right poster- ior root	6	Infection of lower incision and of cord which is al- most severed
111	12/ 6/37	Dorsal 10	120	31A	1/4	Lumbar 2— right ante- rior horn	14	Grossly normal
113	12/ 7/37	Dorsal 9	96	31A	1/3	Lumbar 2— right ante- rior horn	7	Grossly normal
114	12/ 7/37	Dorsal 9	144	31A	1/6	Lumbar 2— linea alba	12	Pus in bladder Otherwise nor- mal
115	12/ 8/37	Dorsal 9	120	31A	1/5	Lumbar 2— linea alba	12	Grossly normal
116	12/ 8/37	Dorsal 9	144	31A	1/3-	Lumbar 2— linea alba	5	Bloody fluid in per- itoneal cavity but no injection of peritoneal sur- faces Bladder distended with bloody fluid
117	12/ 8/37	Dorsal 9	144	31A	1/4+	Lumbar 2— linea alba	7	Grossly normal
164	1/29/38	Dorsal 6	72	678	1/20	Lumbar 3— right linea alba	9	Second incision infected Cord slightly edema- tous
165	1/29/38	Dorsal 3	72	678	1/20	Lumbar 3— right linea alba	6-	Grossly normal

CONTROLS

Three controls with their cords divided in the middorsal region lived for one, two, and three months, respectively. They showed no loss of weight and were finally sacrificed. An additional animal which received one-sixth of a lethal dose of toxin showed no neurologic effects and died on the twenty-ninth day after the second operation.

tetanus toxin into the distal segment of a divided cord produces somewhat different effects from those that follow similar injections into an intact cord. The hind limbs of dogs with spinal cords divided in the middorsal region begin to jerk spontaneously within 20 hours after the introduction of tetanus toxin within the lumbar cord. At this time there is definite tactile, reflex tetanus, the slightest cutaneous stimulation serves to precipitate a series of clonic spasms of the hind limbs. The tendon reflexes are obtainable, and the effort to elicit them brings on a series of jerking, convulsive movements of the lower

half of the body When these animals are held up by a firm grip around the thorax the hind limbs may become quiet, but when the dogs are lying down there is some spontaneous jerking During the second 48 hours the severity and frequency of these clonic movements are increased At the same time some stiffness is noticed in the paralyzed limbs This stiffness is bilateral and increases in severity, occasionally giving rise to an unyielding rigidity In most instances, however, the stiffness can be overcome by steady pressure and the limb completely flexed Stiffness or rigidity of the affected limbs has occurred in every dog with a transected cord Incidentally, these animals afford confirmation of the observations recorded in a previous paper²

All of the animals in this experimental group were given a diet of raw beef, milk, and biscuits In most cases this diet was eaten until the last 48 hours of life, but despite the fact that it was well taken, all of the animals lost a great deal of weight This can be easily accounted for by the constant activity of the dogs In one instance the loss amounted to one-fourth of the body weight in ten days Female dogs were used so as to facilitate the passive emptying of the urinary bladder This was done regularly

All of the dogs with transected cords lived several days longer than those with intact cords, nevertheless, every animal died, despite careful feeding and nursing Dogs with noninjected, transected cords have lived in this laboratory under similar conditions for many weeks without the slightest weight loss

Autopsy of these experimental animals showed no gross changes which would explain death It is not surprising that the action of the toxin in the distal end of a severed cord should be distinctly different from that in an intact cord The physiologic reactions of a severed cord differ greatly from those of the intact cord The significant fact is that all of the animals died without any apparent cause The same observation was made on three dogs in which the dorsal cord was divided four hours after the deposition of toxin into the lumbar cord One of these animals lived for 19 days The frequency and severity of the clonic movements greatly diminished during the last few days of life, and it seemed as if the animal would recover At autopsy there was evidence of a large hemorrhage into the cord at the site of injection, and this may have accounted for the diminished symptoms The animal lost so much weight during the 19 days that it was impossible to draw any conclusions as to the cause of death

Protocol of Typical Experiment—Dog No 165 Adult, female, mongrel, weight 7.2 Kg

First Operation—January 29, 1938, 11 A M Under anesthesia, the operative field was shaved and prepared with iodine and alcohol A laminectomy was performed on the third dorsal vertebra The dura was not opened, but a segment of dura and spinal cord measuring 1 cm in length was excised The bleeding was controlled with packing There was a gap of almost 2 cm between the severed ends of the cord The wound was closed with silk throughout

January 30 There was flaccid paralysis of the hind limbs

Second Operation—February 1, 10 A M Under ether anesthesia, the operative field was prepared as before A laminectomy on the third lumbar vertebra was carried out

The dura was incised in the midline and a denticulate ligament on the right side was divided. The cord was rotated so that the operator could have easy access to the lateral columns. With the special injection apparatus, 0.0026 cc of tetanus toxin, Batch No 678, was placed under the linea alba. There was slight oozing following the puncture. The wound was closed with silk throughout.

February 2. There is beginning jerking of the hind limbs. Tactile, reflex tetanus is present. The bladder was emptied. The dog is eating well.

February 3. Both hind limbs jerk while the animal is lying down. They are held extended but can be passively flexed, the right is stiffer than the left. The tendon reflexes can be elicited on the right but not on the left because of the constant clonic spasms. The animal feels hot. Rectal temperature 105° F. The bladder was emptied. The dog is eating and drinking.

February 4 and 5. There is no change in the animal's condition.

February 6. The animal seems sicker than yesterday.

February 7. The animal was found dead. Autopsy showed the lungs clear, no gross pathologic changes in the abdominal viscera. Both wounds were well healed. There was no sign of wound or urinary tract infection. The cord was not edematous at the point of injection.

EXPERIMENT 4 *Method of Procedure*—Many of the animals that are included in the preceding experiments were unobserved at the time of death. In several instances, however, an effort was made to watch the manner of death, and every time that this was done it was seen that the animal would give several deep terminal gasps. The heart beat was palpable for two or more minutes after all respirations had ceased. In fact, on five occasions the chest was opened and the heart was observed to continue beating from three to five and one-half minutes after the last visible respiratory effort. This observation brought up the question whether or not paralysis of the respiratory centers accounted for the death of the animals in these experiments, accordingly, it was decided to inject minute quantities of the toxin into these centers. Fortunately, Gesell, Bricker, and Magee⁴ had studied the location of the inspiratory and expiratory centers of the dog. The numerous experiments carried out by these investigators prove that the mere introduction of a sharp needle or electrode into the dog's medulla is not followed by any untoward symptoms, nevertheless, we repeated and confirmed this observation. As an added control for the deposition of tetanus toxin into so vital an organ as the medulla, we placed from 0.001 to 0.006 cc of diphtheria toxin, boiled water, toxic serum, or filtrates from colon bacilli, meningococci, Staphylococci (H. A. strain), and typhoid bacilli (Table IV). Only with the first named substance were there any detectable effects upon the well-being or length of life of the animals. Four of the five animals receiving diphtheria toxin into the medulla died within 40 hours. The fifth, which received only 0.0005 cc in a single injection, lived 13 days. The autopsies of the four dogs that received larger amounts of diphtheria toxin showed gross and extensive areas of hemorrhagic necrosis about the site of injection. On the fifth day there was an area of softening 2 to 3 mm in diameter at this site. This animal died from an acute hemorrhagic pancreatitis. It is interesting to note that diph-

theria toxin placed in the lumbar cord produces flaccid paralysis but does not cause death

In all of the animals receiving tetanus toxin in the medulla, there was a latent period during which the dog seemed perfectly well. Even when such an enormous amount of toxin as $1/12$ of a lethal dose was put into the medulla (Dog No 175), the animal remained symptomless for seven hours. Following some of our medullary injections, the latent period has been as long as five days. It is clear that this latent period, or incubation period as it is sometimes called, is proportional to the amount of toxin injected.

The first symptom that is noticeable is difficulty in swallowing. This is soon followed by clonic spasms of the pharyngeal muscles whenever the dog attempts to eat or drink. Later these spasms occur spontaneously. The picture simulates that condition which has been described clinically as tetanohydrophobia. The spasms are not painful and between them the animals remain quiet. In no instance was there any evidence of involvement of the muscles of the trunk or limbs. The time of death varied with the quantity of toxin placed in the brain. When $1/10$ of a lethal dose was injected, the animal died in about 24 hours, whereas, when $1/1,100$ of a lethal amount was used, the dog lived 17 days. On the whole, it seems that death occurs a little sooner following the deposition of toxin into the medulla than into the lumbar cord, but the difference, if any, is too slight to be significant. It is certainly true that the manner of death is the same in both instances, and forms a very great contrast to the manner of death following injections of diphtheria toxin into the medulla, for in the latter group of animals there is no gasping, and the animals are comatose during the last few hours of life and die quietly.

Because of the interference with swallowing we gave glucose solutions and saline parenterally to all the animals that lived longer than 36 hours, but despite these treatments there was always great loss of weight. In the case of dogs with pharyngeal spasms living more than a week, it is impossible to say whether death is due to exhaustion, inanition, or some specific action of the toxin. The data of this experiment are summarized in Tables III and IV.

Protocol of Typical Experiment—Dog No 136 White and brown fox terrier, female, age nine months, weight, 5.3 Kg

Operation—January 5, 1938, 2:30 A.M. Under ether anesthesia, the operative field was shaved and prepared with applications of iodine and alcohol. A dorsal midline incision was made, beginning at theinion and extending for 6 cm. The fascia was divided in the midline and the muscles were retracted. The anesthetist then flexed the animal's head to the greatest possible degree, and the dura was opened from the edge of the foramen magnum to the atlas. Great care was taken when enlarging this incision to avoid tearing into the adjacent venous sinus. After absorbing the excess cerebrospinal fluid with gauze, the operator rongueured away a small piece of the occipital bone and thus obtained good exposure of the medulla. One injection of tetanus toxin was made 2 Mm. to the right of the obex and a similar one on the left side. Each injection amounted to 0.0025 cc. of a $1/50$ dilution of toxin, Batch No 678, and was equivalent to $1/80$ of an intravenous lethal dose. There was no bleeding. The wound was filled with warm normal saline and closed throughout with silk.

TABLE III
INJECTIONS OF TETANUS TOXIN INTO THE MEDULLA

Dog No	Date	Toxin No	Total Dosage in Dog Units	Site of Injection	Remarks	Symptoms	Survival Period in Hours	Autopsy
136	1/ 5/38	678	1/40	Right and left	Given fluids intraperitoneally	Pharyngeal spasms	33	Grossly normal
137	1/ 5/38	678	1/42	Right and left	Only fair exposure Given fluids	Pharyngeal spasms	27	Grossly normal
138	1/ 6/38	678	1/42	Right and left	Delayed appearance of pharyngeal spasms	Pharyngeal spasms	60	Grossly normal
140	1/11/38	678	1/500	Right only	Rough dilution Poor exposure Given fluids intraperitoneally	Typical spasms	216	Grossly normal
142	1/12/38	678	1/450	Right and left	Rough dilution Given fluids	Typical spasms	72	Grossly normal
145	1/12/38	678	1/10	Right and left	Fair exposure	Typical spasms	20	Sacrificed but was moribund Grossly normal
146	1/14/38	678	1/10-	Right and left	Poor exposure	Typical spasms	24	Grossly normal
148	1/18/38	678	1/12	Right and left	Could drink	Slight pharyngeal spasms not typical	48	Liver large and granular
149	1/18/38	678	1/12	Right and left	Good exposure	Typical spasms	24	Grossly normal
166	2/ 2/38	678	1/1,000	Right only	? Needle came out Could not pass stomach tube	Spasms after one week	9 days	Grossly normal
167	2/ 2/38	678	1/1,100	Right only	Ate beef and milk for 4 days	Spasms after 5 days	8 days	Grossly normal
175	2/ 7/38	678	1/12	Right and left	Poor exposure	Typical spasms Vomiting	27	Hemorrhage in substance of medulla along needle track
176	2/ 9/38	678	1/20	Right only	Copious bleeding	Typical spasms Turns to right	22	Grossly normal
178	2/10/38	678	1/23	Left only	Poor exposure	Typical spasms Turns to left	24	Grossly normal

ACTION OF TETANUS TOXIN

TABLE III (Continued)

Dog No	Date	Toxin No	Total Dosage in Dog Units	Site of Injection	Remarks	Symptoms	Survival Period in Hours	Autopsy
188	2/23/38	678	1/1,000	Right and left	Received fluids intra-peritoneally	Typical spasms Barking and growling	140	Liver cirrhotic 70cc bloody fluid in peritoneal cavity Nothing else
189	2/23/38	678	1/1,100	Right and left	Eats well	Barking and growling No symptoms	7 weeks	Sacrificed
190	2/23/38	678	1/2,000	Right and left	Eating until sixth day Wants to but cannot thereafter	Occasional typical spasms	240	Questionable consolidation of lungs probably insufficient to cause death
196	3/18/38	678	1/1,200	Right and left	Got distemper Received fluids intra-peritoneally	Could not eat Had spasms after sixth day	17 days	Consolidation of lungs Lost 30 per cent of weight
197	3/18/38	678	1/2,000	Right and left	Received fluids intra-peritoneally	Did not eat Had typical spasms just before death	148	Died in spasm Some consolidation of lungs

January 5, 10 P M The animal appeared quite normal

January 6, 9 A M When first seen, the animal was quiet, alert, walking about, wagging its tail There was no trismus, no tetanus dolorosus It gave an occasional quick jerk of the head Frequent attempts to drink produced violent clonic spasms of the pharyngeal muscles which lasted 30 seconds Auditory and tactile stimuli did not provoke spasms The knee kicks were present and active, and testing them did not produce a seizure

Twelve noon Temperature, 107.6° F per rectum The dog was given 300 cc of saline and 5 per cent glucose solution intraperitoneally It was observed closely thereafter, until the time of death at 11 30 P M For the first four hours of this period, spontaneous clonic spasms of the pharyngeal muscles occurred at intervals of two to 12 minutes The duration of each was from 15 to 30 seconds Between the attacks the dog was quiet and in no apparent pain At times it would shake its head and had a tendency to incline the head to the right side It frequently scratched its right ear The respirations became increasingly rapid After 4 P M the pharyngeal spasms were interspersed with spells of jerking of the head

At 5 P M another smaller injection of glucose solution was given intraperitoneally Rectal temperature, 105° F, pulse, 160, respirations, 84 The spasms seemed to occur at greater intervals but to last longer The dog died at 11 30 P M The autopsy was negative

EXPERIMENT 5 *Method of Procedure*—The death of dogs under the conditions of the preceding experiments might conceivably result from a multiplication of the toxic molecule within the spinal cord and the subsequent

absorption of a fatal amount of the blood stream. Such a happening is, however, highly improbable because none of the animals showed any peripheral signs of general tetanus. To exclude the possibility of such a mechanism being at work, a number of dogs were given varying amounts of tetanus antitoxin at varying intervals after the spinal injections. It was evident from this experiment that both the amount given and the interval influence the result. A determination of the exact relationships that exist between the proportion of toxin-antitoxin and the interval between injections was not necessary for our purpose. A simpler and more exact experiment was to have the antitoxin circulating in the blood *before* the toxin was placed in the spinal cord. The results of this experiment show clearly that as much as 100 times the neutralizing dose of antitoxin can be circulating in the blood stream at the time of the spinal injection without affecting the symptoms or the time of death. This experiment shows that the death of the animals is not due to multiplication of the tetanus toxin within the spinal cord.

TABLE IV
CONTROLS FOR INTRAMEDULLARY INJECTIONS

Dog No	Date	Material Injected	Amount Injected	Site of Injection	Remarks	Symptoms	Survival Period
118	1/ 5/38	Boiled water	0.004 cc	Right and left		None	Indefinite
122	1/ 5/38	Boiled water	0.004 cc	Right and left	Slight trauma to cord	None	Indefinite
124	1/ 6/38	0	0	Right and left	Inserted needle	None	Indefinite
154	1/21/38	B. coli toxin	0.004 cc	Right and left	Good exposure	None	Indefinite
155	1/21/38	Meningococcus toxin	0.004 cc	Right and left	Good exposure	None	Indefinite
159	1/25/38	H. A. Staphylococcus toxin	0.004 cc	Right and left	Good exposure	None	Indefinite
162	1/27/38	B. typhosus toxin	0.006 cc	Right and left	Good exposure	None	Indefinite
163	1/27/38	Meningococcus toxin	0.006 cc	Right and left	Good exposure	None	Indefinite
179	1/12/38	Diphtheria toxin	0.006 cc	Right and left		Not seen	20 hours
180	2/15/38	Diphtheria toxin	0.002 cc	Right only		Cannot stand No jerks etc	27 hours
181	2/15/38	Diphtheria toxin	0.003 cc	Right only		Turned somersaults in cage for short period	40 hours
186	2/17/38	Diphtheria toxin	0.001 cc	Right only		Not seen	23 hours
187	2/17/38	Diphtheria toxin	0.005 cc	Right only		None	13 days
194	2/28/38	Toxiferous blood	0.006 cc	Right and left		None	Indefinite

EXPERIMENT 6 *Method of Procedure*—After establishing the fact that intraspinal injections of minute amounts of tetanus toxin cause death, we attempted to study the effects of introducing still greater dilutions of the toxin. An abstract of the data on six dogs which received intramedullary

injections of 1/1,000 or 1/2,000 of an ordinary lethal dose is given in Table IV. These dogs had clonic pharyngeal spasms and lived from six to 17 days. Because of the interference with swallowing, it is impossible to attribute their death to the action of any secondary substance. There were eight other dogs in which the toxin was put into the white matter of the lumbar cord. The first four of these dogs were given approximately 1/1,000 of a lethal dose, and except for a slight transient weakness in gait, probably due to trauma, they showed no effects from the injections. There were no significant changes in the superficial or deep reflexes, and no evidence of clonic spasms. In this respect the injections of toxin into the white matter of the lumbar cord differ from those into the medulla. This difference is probably due to the toxin reaching a larger number of motor cells following medullary injections than after lumbar injections. This experiment will have to be repeated on a larger series of animals and be combined with careful histologic studies before it can be used as an argument that tetanus toxin has no effect on the white matter of the cord. The four remaining dogs were given 1/500 of a lethal dose in the lumbar cord. Two of these showed no symptoms attributable to the toxin. The third died with typical spasms on the fourth postoperative day. The autopsy was negative. The fourth dog was most interesting. It was given two injections of 0.0025 cc each of a 1/50 dilution of toxin, Batch No. 678, into the right side of the lumbar cord. During the next four days there were no significant symptoms. On the fifth day the right hind leg jerked constantly when the animal was standing. There was difficulty in walking. The knee kick on the left was normal but could not be tested on the right because of the constant clonic movements. The cutaneous reflexes on the right were increased. There was no stiffness. This state of tactile, reflex tetanus continued for three days, at which time the jerking gave place to tremors, which lasted four days. Thereafter the dog remained entirely well.

This animal is the only one that recovered after having unmistakable clonic spasms. It corresponds, we think, to dogs receiving from one-half to three-quarters of a lethal dose intravenously, for in these animals signs of descending tetanus develop but the dogs recover. When less than one-half of a lethal dose is given intravenously (or into the spinal fluid), no symptoms occur. It seems that the corresponding ineffective dose for lumbar injections is less than 1/500 of the intravenous dose.

Pathology—The report of these experiments would be incomplete without some word concerning the pathologic alterations that result from the introduction of tetanus toxin into the medulla and spinal cord of dogs. Grossly, one sees only a thin blood clot along the puncture wound made by the needle. No edema has been observed nor any visible inflammatory reaction. Histologically there are definite cytologic alterations. These are best seen in the medullary specimens but are essentially the same in other parts of the cord. The alterations are surprisingly well localized to the site of injection. The adjacent cranial nerve nuclei are apparently unaffected. There is a slight polymorphonuclear infiltration about the lesion and around the neighboring

blood vessels The needle tract is outlined by cells which seem to be microglia The endothelium of the blood vessels is intact and there are no evidences of thrombosis Another alteration is the presence of large numbers of phagocytic cells, apparently macrophages The third change is in the nerve cells Here one finds changes in the Nissl substance, which seems pale and granular This change can be best described as chromatolysis The nuclei of some of the cells are irregular, swollen, and distorted A few of the nerve cells are dead, others appear viable but altered With fiber stains one finds great alteration in the myelin, but this observation has to be interpreted with caution since the specimens were not fixed immediately upon the death of the animals In order to really trace the sequence of cytologic alterations, a special study with the vital staining technic is now being carried out In this an effort is being made not only to eliminate changes resulting from delayed fixation, but also to determine how much of the pathologic picture is due to trauma, how much to the presence of a foreign substance, and how much may be looked upon as the specific action of the toxin

Discussion—From the foregoing experiments it seems clear that tetanus toxin causes death when placed in the dog's spinal cord This result ensues after the deposition of as little as 1/500 of the ordinary lethal dose In several experiments we placed fractions of a lethal dose in the sciatic nerve, an anterior and a posterior nerve root, the adrenal, and the brain without any noticeable effect This last organ was injected in six dogs Twice the motor cortex was identified by electrical stimulation before placing the toxin in it In not a single dog could one detect the slightest visible reaction to the toxin This observation is in keeping with the clinical picture of tetanus, which is singularly free from cerebral symptoms The fact that death occurs despite the introduction of the toxin into a nonvital center and despite the severance of the cord above the point of injection, points to the conclusion that tetanus toxin is altered in the spinal cord to form a new substance that is absorbed by the blood stream and causes the death of the animal That this new substance is not susceptible to the neutralizing action of tetanus antitoxin is shown by Experiment 5, in which the presence of 100 neutralizing doses of antitoxin in the blood stream failed to prolong life

The concept that tetanus toxin is altered in the spinal cord is not a new one Forty years ago, Courmont and Doyon⁵ suggested that central nervous system symptoms of tetanus do not appear until the toxin has been changed into a strychnine-like body The concept that this secondary substance is a cause of death is new In addition to the experimental data presented in this paper, there are two other observations that lend weight to the correctness of this concept The first is the fact, well known to all investigators of the disease, that it is impossible to demonstrate the presence of tetanus toxin in the spinal cord of animals dying from tetanus, despite the preponderance of spinal cord symptoms In commenting upon the fixation of toxin by the spinal cord after intravenous injections, Doctor Abel has recently expressed this fact by saying that "neither the bio-assay nor any other method now at

our disposal enables us to detect and assay this fixed fraction of the injected toxin."³ It seems that the inability to detect the toxin can well be explained by its alteration

The second fact is that tetanus antitoxin is of no avail in experimental animals receiving one or more lethal doses of toxin intravenously if it is given after central nervous symptoms appear. Abel and Chalian⁶ have recently studied the length of time in which antitoxin is effective after varying amounts of toxin given intravenously. They have shown, for instance, that following three intravenous lethal doses, one can save the dog with antitoxin up until the appearance of central reflex symptoms. With larger doses there is a shorter period in which antitoxin is effective. This insusceptibility of toxin to antitoxin, once fixation and incubation have taken place, can be looked upon as additional evidence of its alteration.

SUMMARY AND CONCLUSIONS

A technic has been devised for the accurate injection of minute amounts of tetanus toxin into various parts of the dog's spinal cord. By this procedure it is possible to produce pure reflex motor tetanus without the slightest evidence of muscular rigidity. As little as 1/2,000 of an intravenous lethal dose placed in the medulla suffices to bring on reflex motor spasms of the pharyngeal muscles. The intraspinal injection of 1/400 or more of the usual intravenous lethal dose of tetanus toxin has always been followed by the death of the animal, despite the fact that the toxin was placed in a nonvital center such as the lumbar cord. The explanation that death results from an upward passage of the toxin is untenable because transection of the cord above the site of injection does not prevent death. Similarly, division of all sensory and motor pathways below the lesion is without effect. The death of the animal cannot be caused by a multiplication of the tetanus molecule and subsequent reabsorption because the presence in the circulating blood of 100 neutralizing doses of antitoxin does not prevent a fatal outcome. The tentative explanation put forward to account for the results obtained in the foregoing experiments is that tetanus toxin is altered in the spinal cord to form a secondary substance that is responsible for the dog's death.

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DISCUSSION—DR PETER HEINBECKER (St Louis, Mo) The authors, by using minute amounts of tetanus toxin injected directly into the cord, have apparently been able to separate local from clonic tetanus. This is an unusual physiologic feat. Apparently, the dosage was just adequate to bring about a facilitation for those reflexes initiated by the afferent fibers concerned in clonic reflexes, but not sufficient to facilitate appreciably the mechanism for proprioceptive reflexes concerned in local tetanus.

I am unable to accept the interpretation that local tetanus is a manifestation of alteration in the muscle itself. I adhere to the view that both local tonic and clonic tetanus are an expression of influence of the toxin on the central nervous system.

The problem of the potentiation of tetanus toxin on injection into the spinal cord is a difficult one to analyze. In 1933, Condrea and Poenaru produced evidence that tetanus toxin was modified by the diluent into which it was placed prior to injection. They found that the toxic effect increased remarkably when the toxin was united with peptone. Recently, a report has been issued by Zuger and Friedemann, in which they stated that there was a potentiation of tetanus toxin on mixing it with muscle *in vitro*. It is possible that such a potentiation was here also due to admixture with a substance like peptone, which increased the rapidity with which the toxin reached the vital centers. There was no evidence in any of their experiments to indicate that the amount of toxin was altered, because, *in vitro*, no additional antitoxin was required to neutralize the toxin mixed with peptone or muscle.

Rivers mixed tetanus toxin with spinal cord tissue and found that the amount of antitoxin required to neutralize it, *in vitro*, was even less than that required to neutralize the toxin alone. However, Doctor Firor informs me that after incubation, such a mixture of toxin with cord does result in a potentiation of the mixture. It is possible that in his experiments in which injections were made into the cord, slight injury resulted, and the body, acting as an incubator, permitted the development of a substance which when mixed with the toxin permitted a more rapid penetration into the vital areas than when the toxin alone was present. However, I am not certain that this is the explanation, and I feel that Doctor Firor will have to present very excellent evidence to show that a new substance has been formed, a new toxin, before the idea can be accepted.

I consider the method of action of tetanus toxin to be similar to that of strychnine on the central and peripheral nervous system. Strychnine acts by lowering the threshold for nervous excitation and it also acts by altering accommodation of the nervous system to stimuli. By that, I mean that ordinarily nerves, and presumably cells, tend to fail to respond to a prolonged stimulus after a certain period of time. We have found in our laboratory that in the presence of strychnine such a failure to respond does not occur, and I consider the activity of tetanus toxin to be very similar to that of strychnine.

I think the manner of death by tetanus to be one of exhaustion, exhaustion of the muscles from continued stimulation arising in the central nervous system. There is no evidence of a failure of the central nervous system. The muscles just tire and fail to respond. Realization of this point will guide us in our therapy. We can organize a rational form of therapy.

I have one graph which I would like to show. Some weeks ago, Doctor Firor talked to me about this subject and I told him that I could present an illustration indicating how strychnine acted upon the central nervous system, and possibly reveal how tetanus toxin acts.

Figure 1, 3A is a record of the activity of the phrenic nerve in a curarized animal. You see, there is a series of impulses coming down, then there is a

ACTION OF TETANUS TOXIN

pause, and during the next respiratory effort, another series of impulses will descend. After strychnine, we get the type of activity shown in Figure 1, 3B. The central nervous system fails to accommodate and one gets long-continued activity.

When, as shown in Figure 1, 4, you record the activity in the sciatic nerve of such a curarized animal, it will be found that on very slight stimulation of the saphenous nerve, a series of responses is obtained. This would represent ordinary tactile stimulation. When the animal is stimulated a little harder, a long-continued series of responses results. It is the effect of such a continued action of the nervous system on muscles which leads to fatigue and is, in my mind, the cause of death.

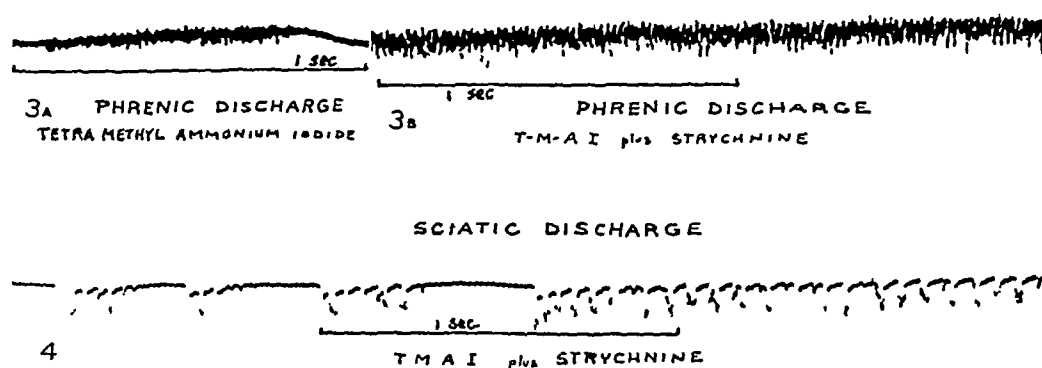


FIG 1—(3A) Graph showing phrenic discharge in a curarized animal
(3B) Result on phrenic discharge after administration of strychnine
(4) Result on sciatic discharge after administration of strychnine

One other interesting point here—because this animal is curarized, we do not get proprioceptive impulses from the periphery, so that we have absolutely smooth intervals in our record. Such an animal, being entirely without tone, does not show the electrical evidence of proprioceptor reflexes which one obtains in the ordinary animal.

DR WARFIELD M. FIROR (Baltimore, Md.) closing: I want to thank Doctor Heinbecker for his discussion and for his healthy incredulity. I think he is absolutely right in saying that one must offer excellent evidence before he can assume that a second toxin is formed, because this is a very unphysiologic concept—the body steps up the potency of a lethal agent for its own destruction.

I disagree, however, with Doctor Heinbecker, that fatigue is the cause of death, because in the series of animals in which we divided the conus and the lumbar nerves, there were no muscular contractions, there was no muscular activity. Nevertheless, these animals died in exactly the same manner and the same time as those that suffered from very violent muscular activity.

I am glad also that he brought up the point about the spinal cord experiments of Doctor Rivers. I may say in passing that you will note in the abstract a mention of four dogs in which tetanus toxin was injected into the lumbar cord and then, just before death, that segment of the cord was excised and injected into healthy dogs, and caused their death. We have not included that experiment in this particular communication because we have been able to obtain that result in only five out of 20 experiments, and do not think that such a proportion is statistically significant. Nevertheless, one has to explain the death of those five animals, and the experiments which we are now conducting will, I think, shed light on that point and will also offer the indisputable proof that Doctor Heinbecker wants.

BOOK REVIEW

THE HORSE AND BUGGY DOCTOR By Arthur E. Hertzler, M.D., New York and London Harper & Brothers, 1938

The reviewer takes the greatest satisfaction in unequivocally praising the latest effort of Doctor Hertzler after having read the recitation of his life struggle. This biography should be read by both young and old, by the former to stimulate them to emulation and by the latter to afford them the pleasure of learning what has been accomplished by a man who has passed through certainly more than his share of vicissitudes, many of which must bring back to the reader similar situations in his own life. The book will certainly prove to be most interesting to lay people as well as to members of the medical profession. This is reflected if one consults the tabulation of the books America is reading as summarized in the weekly reviews of those most popular, in which it has risen rapidly to second place.

The author has injected a most interesting personal philosophy throughout the book, admixed with a remarkable, homely humor, at times salty, in which one can readily appreciate the reputation he has earned as a most amusing raconteur. Indeed, a little of the "Hertzlerian" humor would make anyone feel better and a continuation of it would effect a cure in a great many patients.

The almost incredible experiences through which Doctor Hertzler passed from boyhood to his present prominent position, are interestingly and fascinatingly recited, illustrating, by example, his triad for success, namely, the material, the books and *the will to do*. His progression in life is concisely indicated by the twelve chapter captions: "Medicine as It Was in My Boyhood, I Prepare to Study Medicine, I Study Medicine, I Go to the Patient, I Arrive at the Patient's Bedside, The Patient Comes to the Office, I Seek Further Education, I Educate Myself, I Practice Kitchen Surgery, I Build a Hospital, Me and My Patient, Medicine as It Is To-Day."

I do not recall ever having read a more absorbing story than that detailing his experiences in performing "kitchen surgery." It shows what can be accomplished with practically no facilities by one gifted with unusual common sense, adaptability, ingenuity, resourcefulness, determination and daring, when backed up by the preparation which the author had so laboriously acquired. The subject matter itself is most amusingly presented and the details of cases reported really thrilling.

That "a man may be known by the company he keeps" may be remarked by the friends with whom Doctor Hertzler associated himself, veritably acquiring a postgraduate education on a "shoestring." Are not the names of Jaggard, Fenner, Dean, Davis, Hans Virchow, Waldeyer, von Bergman, Fischer, Kopsch, Janzen, Lexer, Gerhardt, Juergens, Lassar, *etc*, *etc*, ones to conjure with? An imposing shelf of some thirty-odd scientific works by

Doctor Hertzler is sufficient evidence of the knowledge gained from, and the impetus given by these teachers and well exemplifies his chief desideratum, "*the will to do*"

His characterizations of operative assistants are most amusing and ironical. His conclusions relative to wound infections, as gathered from his own observations under most adverse conditions, are well worth considering seriously. They are certainly quite at variance with some of the present-day ideas. His unfortunate experiences with the establishing of a private hospital are pathetic, they will be appreciated by many of his readers who have passed through the same trials.

Thus, one could continue *ad infinitum*, so many are the interesting and important questions introduced by Doctor Hertzler, but one's own "Horse and Buggy" probably, it is hoped, waits.

To summarize and conclude, therefore. Read it as soon as possible, then reread much of it and find out what you missed of its context and philosophy the first time.

JAMES T. PILCHER

BOOKS RECEIVED

THE receipt of books for review is hereby acknowledged. This statement shall be regarded as sufficient acknowledgment of the courtesy of the publishers. Selections will be made for review predicated upon the interests of the readers of the ANNALS OF SURGERY and as space permits.

THE PRACTICE OF UROLOGY By Leon Herman, M D Philadelphia and London W B Saunders Co, 1938

EMERGENCY SURGERY By Hamilton Bailey, F R C S (Eng) Baltimore William Wood Co, 1938

THE PRINCIPLES AND PRACTICE OF MEDICINE By Henry A Christian, M D, LL D, F R C P 13th ed D Appleton-Century Co, Inc, New York and London, 1938

CLINICS ON SECONDARY GASTRO-INTESTINAL DISORDERS By Julius Friedenwold, M D, Theodore H Morrison, M D, and Samuel Morrison, M D Baltimore William Wood Co, 1938

INTERNSHIPS AND RESIDENCIES Report by New York Committee New York The Commonwealth Fund, 1938

THE VITAMINS AND THEIR CLINICAL APPLICATIONS By Doctors Stepp, Kuhn and Schroeder The Wisconsin Cuneo Press, Inc, 1938

THE HORSE AND BUGGY DOCTOR By Arthur E Hertzler, M D Harper and Brothers, New York and London, 1938

INDUSTRIAL SURGERY By Willis W Lasher, M D New York Paul B Hoeber, Inc, 1938

MANAGEMENT OF FRACTURES AND DISLOCATIONS, Edited by Philip D Wilson, M D Analysis of 4,390 cases of fractures and dislocations treated at the Massachusetts General Hospital, 1923-1930 Philadelphia J B Lippincott Co, 1938

THE 1938 YEAR BOOK OF PHYSICAL THERAPY, Edited by Richard Kovacs, M D The Year Book Publishers, Inc, Chicago, 1938

HUMAN PATHOLOGY By Howard T Karsner, M D 5th Ed Philadelphia J B Lippincott Co, 1938

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THE TREATMENT OF BRAIN ABSCESS *†

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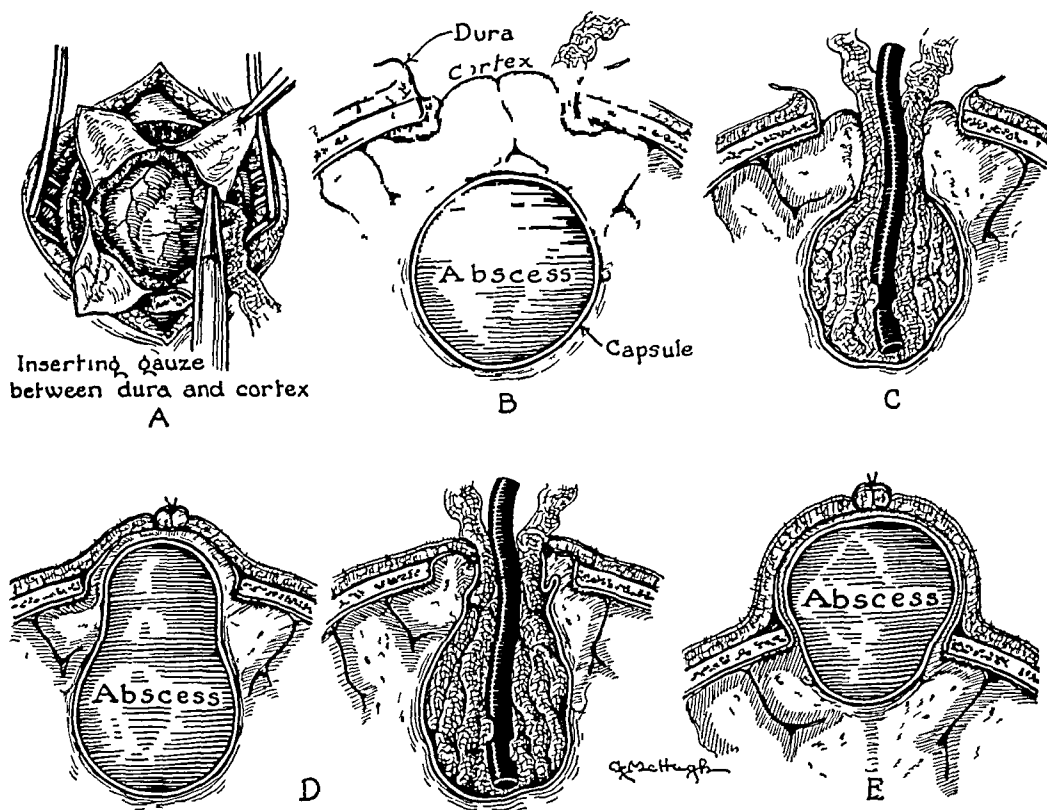
THE most appropriate method of dealing with abscesses of the brain is still the subject of discussion. Any method which has proved reasonably successful merits consideration. The present report is based upon a series of 17 consecutive cases in which the abscess has been dealt with surgically (Table I). Of the 17 cases, four were cerebellar and 13 were cerebral †. Of the former none died. Of the cerebral cases five died (29.4 per cent). In three of these five fatal cases the infection metastasized from the lung. In Case 2, there were multiple areas of infection throughout the body, in the chest, abdomen and pelvis, and a culture of the blood revealed *Staphylococcus aureus*, the organism found in the cerebral abscess. The patient improved greatly following drainage of a large abscess in the right parietal area, only to become unexpectedly stuporous on the eighth postoperative day and die within 24 hours. Knowing the tendency for abscesses which originate by metastasis from the lungs to be multiple, it was believed that death was probably the result of one or more other intracranial abscesses. Unfortunately, necropsy was refused. In Case 3, a child of 18 months, where the infection also arose from the lung, necropsy revealed a total of seven separate, intracerebral abscesses and a leptomeningitis. In Case 5, the child, age 3, was admitted in extremis, and died within less than 24 hours after admission and operation. Necropsy revealed an enormous abscess of the left parieto-occipital region which had ruptured into the lateral ventricle and produced a diffuse leptomeningitis, in all probability prior to the operation. It is difficult to see how any type of treatment could have benefited these three cases (unless in Case 5, a combination of drainage and the administration of sul-

* Presented before the Chicago Surgical Society, May 6, 1938. Submitted for publication April 21, 1938.

† Since preparing this paper an additional case has been treated and has recovered. The patient (F. S.) was a female, age 4, who had developed a right cerebellar abscess, apparently secondarily to a transitory right otitis media. Hemolytic Streptococci were recovered from the abscess. It was successfully treated with a single aspiration and the subsequent administration of sulphanilamide.

phanilamide which, however, did not exist at that time, 1932, might have proved effective) The other two fatal cases (Cases 9 and 13) presented entirely different conditions and will be considered in detail later

Method Employed—Since 1935, an endeavor has been made to treat all cases by the following method Occasionally, as in Case 12, circumstances have precluded following this procedure completely or, as in Case 8, have made it unnecessary No claim is made that the method is either new or original, only that it seems rational and, as will be seen, has been successful



TWO STAGE METHOD OF TREATING BRAIN ABSCESSES

FIG 1—First Stage (A and B) An incision and small craniectomy are made over the abscess. A cruciate incision is made in the dura mater, and the subdural space about the opening is packed with gauze soaked in a weak solution of iodine.

Second Stage (C) The usual finding at the second operation. The cerebral cortex has been sealed to the dura mater. The cortex overlying the abscess is removed and the abscess is evacuated and drained. (D) When the abscess has partially herniated through the craniectomy it can be marsupialized and drained. (E) Rarely, the abscess will be found to have herniated out or the skull. It can then be removed *in toto*.

First Stage—The abscess having been localized, an incision is made over it. In the case of a cerebellar abscess of otogenic origin, the incision is a vertical one, made a short distance medial to the mastoid process and the wound of the mastoidectomy, with an otogenic abscess of the temporal lobe, the incision is just in front of the ear. The margins of the incision are separated by a self-retaining retractor. A trephine opening is made in the skull and enlarged with a rongeur to 3 or 4 cm in diameter. A cruciate incision is made in the dura mater. The resultant triangular flaps of dura mater are

reflected exposing the tense and bulging cerebral cortex. A long strip of one-half inch selvedged gauze is soaked in one-fourth strength tincture of iodine and lightly dried with a gauze sponge. This gauze strip is then packed into the subdural space beneath the dura around the margins of the opening (Fig 1 A and B). In doing so the pia-arachnoid membrane and cerebral cortex are moderately traumatized. If the patient's condition is satisfactory, nothing further is done and the wound is closed, bringing the end of the gauze strip out through the incision. If the patient is suffering from severely increased intracranial tension, a needle is inserted through the cortex into the abscess, after the subdural space has been walled off, and as much pus as will, allowed to escape. The needle is then withdrawn and the wound closed.

This method is designed to close off the meningeal spaces, subdural and subarachnoid, from the infectious material escaping from the abscess. It has long been recognized that the tendency for the brain to fall away from the dura as the abscess is evacuated opens these channels and is a great potential source of meningitis, usually a fatal complication. This method which deliberately promotes scar formation between the cerebral cortex, pia-arachnoid membrane and dura mater prevents this. It has been adopted from the thoracic surgeons, who utilize a similar procedure to obliterate the pleural space about the site of drainage of a lung abscess. Its success in the field of thoracic surgery is well known. Although it has been used by other surgeons, as noted by Davidoff,³ the usefulness of the method is not commonly recognized. Some neurosurgeons attempt to wall off these spaces by cauterizing the dura mater and by suturing it to the pia-arachnoid membrane and then draining the abscess at the same operation (Adson and Craig,¹ and Davis⁴). Knowing the insecurity of sutures placed in the pia-arachnoid and the tenuous nature of adhesions produced by the dead coagulum resulting from the electric cautery, this method has been avoided in this clinic. The use of a two stage procedure, but without any mechanical or chemical stimulus to promote obliteration of these spaces, was advocated by Dowman, in 1923,⁵ but not generally accepted.

In only one case have we had an opportunity to examine the meningo-cerebral scar produced by this method. As the case itself is unusual and interesting, it is presented in some detail.

Case 13—Unit No 191568 N. A. C., female, age 6, was referred by Dr J. R. Doty of Gary, Indiana, with the diagnosis of a brain abscess. She was admitted to the University of Chicago Clinics January 24, 1938.

On November 1, 1937, the patient fell while playing, forcing a long dried weed up her right nostril. There was profuse bleeding but no other symptoms at the time. That night she vomited and complained of headache. Subsequently she had repeated episodes of headache and vomiting, which usually occurred in the early morning. The symptoms grew steadily more severe. The child lost weight, her appetite was poor and she became irritable. She was in bed during most of the month of January. There was no fever until January 16, 1938, when she developed a temperature of 103° F.

Some fever was present thereafter. On January 21, 1938, she developed a severe headache, vomiting and a stiff neck which persisted.

Physical Examination—She was poorly nourished and dehydrated, and, although rather listless and irritable, was fairly cooperative, rational and well oriented. The superficial veins of the scalp in the right frontal region were dilated. There was marked stiffness of the neck. Kernig's sign was positive bilaterally. There was a severe bilateral papilledema with several hemorrhages. The visual fields were full to gross tests. There was a marked lower, left facial weakness. There was questionable slight weakness of the left arm (she was said to be left-handed) but no weakness in the lower extremities and no evidence of an aphasia. Tendon reflexes were active and equal on the two sides. There was a positive Babinski's sign on the left side. The



FIG 2—Case 13. Drainage of an abscess in the right frontal lobe. The dura mater is firmly adherent around the margins of the site of drainage. There has been no spread of infection to the neighboring meningeal spaces.

temperature was 37.5°C , pulse 60, and respirations 16. *Diagnosis* Abscess of the right frontal lobe.

Operation—*First Stage* January 24, 1938. Under local anesthesia, an incision was made in the right frontal region parallel to and just back of the hair line. A trephine opening was enlarged to 3.4 cm in diameter. The dura was incised and the cerebral cortex, which was under very great tension, herniated through the opening. The subdural space was packed. A brain puncture needle, inserted through the cortex, encountered the abscess at 2.5 cm. Forty-five cubic centimeters of pus were removed. The patient's pulse immediately rose from 60 to 90 per minute. Cultures of the abscess revealed hemolytic *Staphylococcus aureus* and pneumococcus, Type XXIV, for which there is no antiserum.

During the days which followed her pulse varied from 100 to 140, temperature remained about 38°C , respirations 20 to 26. Her condition was good. She ate and took fluids well.

BRAIN ABSCESS

On January 26, 1938, the subdural pack was removed. Two days later a needle was introduced through the incision into the abscess and 17 cc of pus were removed. Cultures revealed that the pneumococci now predominated. On the evening of January 29, 1938, the temperature rose to 39° C.

Second Stage—On January 30, 1938, the wound was reopened. There was considerable infection of the scalp, which was drained. The abscess had herniated through the defect in the bone for a distance of 1.5 cm. The abscess was incised and its contents evacuated. A piece of weed was recovered from within the abscess. The abscess occupied most of the right frontal lobe and measured 7 cm in diameter. The capsule was sutured to the scalp (Fig 1 D) and the cavity packed and drained. The capsule was subsequently, she was much improved and the next day her temperature was normal (37° C) for the first time since her admission. However, that evening at



FIG 3—Case 13. Photomicrograph of the point of adhesion of the dura mater to the cerebral cortex. The dura mater is united to the cortex by a firm scar. The defect through which the abscess was drained is at the right. (Perdrau's method)

6 P.M. her temperature suddenly rose to 40.7° C. The pulse increased from 100 to 164 and she became much more irritable. The wound was examined and seemed all right. There was no drainage of cerebrospinal fluid. A lumbar puncture was made. The fluid was opalescent and contained 4,060 cells which were almost all polymorphonuclear leukocytes. Cultures showed pneumococci. She was given sulphanilamide, fluids were forced and lumbar punctures were made three times daily. The spinal fluid gradually became less purulent but yellow in color, and after February 7, 1938, it was difficult to obtain more than a few cubic centimeters. A block had developed in the spinal subarachnoid space. Beginning February 3, 1938, the number of pneumococci in the spinal fluid began to diminish and by February 5, 1938, cultures of the fluid were sterile. However, her condition grew steadily worse and she died February 10, 1938. *Necropsy* revealed the abscess in the right frontal lobe. The anteromedial part of the lobe was hemorrhagic and degenerated and very adherent to the cribriform plate on that side. When it was removed a portion of the weed was found projecting through

the cribriform plate from the nose into the cranial cavity. There was no evidence of meningitis over the convexity of the cerebral hemispheres or about the site of drainage of the abscess to the margins of which the dura was firmly adherent (Fig 2). There was a thick layer of pus covering the hypothalamus, the undersurface of the pons and medulla oblongata. The infection had obviously spread backward from the region of the cribriform plates and not from the point of drainage of the abscess.

Figure 3 is a photomicrograph of the meningocerebral scar at the edge of the defect in the frontal lobe through which the abscess was drained.

Comment—Although this case terminated unfortunately from a complication which could hardly have been foreseen or prevented, it demonstrates the adequacy of the method for the purpose for which it was designed. The dura was firmly sealed about the site of drainage and this sealing prevented the spread of infection at this point and effectively walled off the meningeal spaces from the infectious material (Figs 2 and 3).

On one occasion (Case 12) the abscess was situated only 3 or 4 Mm beneath the cortex. The subdural space was walled off as usual, but on puncturing the abscess with a needle it ruptured into the field, necessitating evacuation and drainage (as will be discussed below) at the initial operation. Although a most satisfactory result was obtained in this case, it is thought that the one stage procedure is too hazardous to warrant general use. In Case 8, the attack upon the intracerebral abscess was preceded by the removal of a focus of osteomyelitis in the skull and the evacuation of a large extradural abscess five months earlier. The two stage procedure was not necessary as this inflammatory process had walled off the subdural space.

If in the interim between the first and second stages signs of pressure develop, the abscess may be punctured and evacuated. In our experience, however, repeated evacuation through a needle will not suffice to cure an abscess which is not sterile. There may rarely occur cases in which repeated evacuation in this manner will not suffice to relieve tension and the delay necessitated by the two stage procedure may prove dangerous. It is believed that this may have been true in the following case.

Case 9—Unit No 154484 V D, female, age 15, was taken ill, April 27, 1936, two months prior to admission, with a sore throat, chill and fever. Five days later pus began to discharge from both ears. Six days after this a right mastoidectomy was performed at another hospital and pus containing hemolytic *Streptococci* recovered. A week later the left mastoid was opened. The same organism was found. Eight days after this last procedure the patient had a chill, a temperature of 104° F, and *Streptococci* were recovered from the blood stream. A lumbar puncture performed three days later revealed a "normal" pressure, six cells, and Pandy's test was negative. The following day she developed pain in the left temple and about the left eye. The left mastoidectomy wound was reexplored but nothing unusual was found. The subsequent course was uneventful and she was discharged from the hospital three weeks later. She soon developed headache and began to vomit. These symptoms grew progressively more severe. A lumbar puncture demonstrated an increased pressure, 180 cells per cu Mm, mostly lymphocytes, and Pandy's test gave a one plus reaction. She was then admitted to the University of Chicago Clinics, five days after discharge from the other

hospital and two months after the onset of the initial infection, complaining of headache

Physical Examination—The patient was mentally clear and alert. There was an early bilateral papilledema. The neck was slightly stiff. There were slight incoordination and weakness of the left arm. Blood pressure, 115/80. The examination was otherwise negative. The following day her headache was severe. Pulse had fallen to 52 per minute and she soon became comatose. A slight left facial weakness could be made out.

Operation—Nine A M, June 28, 1936. An incision and trephine opening were made in the right temporal region. The opening was enlarged with a rongeur to between 3 and 4 cm in diameter. A cruciate incision was made in the dura and the brain herniated through the opening. A strip of gauze saturated with a weakened tincture of iodine was packed into the subdural space about the opening. A brain puncture needle was inserted and encountered the abscess at 2 cm. Ten cubic centimeters of pus flowed from the needle. Culture showed hemolytic *Streptococcus*. The wound was closed without further intervention. Subsequently, the patient became conscious and mentally alert. The pulse rose to 80. At 10 P M headache returned and the pulse fell to 68. At 5 A M the following morning the pulse fell to 50. Blood pressure, 130/80. The patient complained of considerable headache but was not stuporous. A needle was inserted but only 3 cc of pus were obtained. Although her condition was much improved, it was decided to evacuate and drain the abscess later that morning. At 7 30 A M the pulse was 68, blood pressure, 130/70. At 8 A M the patient suddenly lost consciousness and respirations ceased. The pulse was 114, blood pressure, 194/150. She was immediately given artificial respiration. An unsuccessful attempt was made to puncture the abscess again. The patient was immediately reoperated upon. The opening in the temporal bone was enlarged. The abscess and a portion of the temporal lobe herniated into the field. They were removed. The pulse fell to 88 but spontaneous respiration was not resumed. She was placed in a respirator but died at 6 30 A M the following morning without regaining consciousness. Necropsy revealed that the abscess had been completely removed. There was a very severe cerebral edema and an acute purulent leptomeningitis.

Comment—Of all our cases, this is the only one in which there is the slightest reason to believe that the delay, consequent to the two stage procedure, may have been responsible for the fatal outcome. Even here there is no assurance, in view of the fulminating course and the presence of an acute purulent meningitis at necropsy, that evacuation and drainage of the abscess at the first operation, less than 48 hours before death, would have produced a more fortunate result.

Usually, however, the patient's condition improves during the interval between the two stages. Forty-eight hours after the initial operation the gauze strip is removed permitting the tissues traumatized by mechanical and chemical means to come together and unite by scar formation. Approximately six days after the initial operation the second stage is undertaken.

Second Stage—The procedure at the second operation naturally varies somewhat with what has taken place in the interval and with the findings at that time. In the great majority of cases the abscess will still be found beneath the cerebral cortex and will be treated by incision and drainage (Fig 1 C). In a few instances the abscess will have migrated outward so that the dome protrudes through the defect in the skull (Fig 1 D). These can

best be treated by marsupialization as advocated by Horrax⁶ Still more rarely, the abscess will have migrated through the defect in the skull (Fig 1 E) and can be readily enucleated as recommended by Kahn⁷

Drainage—Usually at the second operation the cortex will be found herniated through the defect in the skull The brain has become firmly sealed to the dura mater about the opening The overlying cortex is removed either with suction or the high frequency electric cautery, exposing the surface of the abscess The dome of the abscess is incised The pus within is removed by suction, care being taken to avoid traumatizing or tearing the capsule After insertion of ribbon retractors into the abscess, the interior can be investigated for evidence of neighboring communicating abscesses A firm rubber drain, 1 cm in diameter, is then inserted into the abscess cavity and held in place by suturing it to the skin The remainder of the cavity is filled loosely with selvedged gauze which is also brought out and sutured to the skin edge The skin is then closed about the drain This method of dealing with the abscess is identical with that advocated by Adson and Craig¹ The same method is equally adaptable to both cerebral and cerebellar abscesses, and there is little or no danger of contaminating the meningeal spaces, a very real danger in any one stage procedure Within 24 to 48 hours removal of the gauze strips is begun, part being drawn out and removed each day After removal of the gauze the rubber drain is released from its anchorage to the skin It will be forced out gradually as the capsule collapses The drain is cut off each day as it is extruded The time and rate of removal of the rubber drain will depend upon the rate of healing of the abscess as determined by the amount of drainage and rate of extrusion of the tube The following case reports will exemplify the method in a cerebral and in a cerebellar abscess

Case 11—Unit No 168171 I G, female, age 7, was referred to us by the Children's Memorial Hospital, Chicago, where she had been admitted January 7, 1937 Two weeks previously she had developed an upper respiratory infection which was complicated by an infection in the right ear On January 9, 1937, a simple right mastoidectomy was performed but no pus was found and she did not improve Six days later the wound was reexplored and pus was obtained from cells in the zygomatic region Two days later, January 17, 1937, she developed a severe headache Examination revealed a bilaterally positive Kernig's sign, a left Babinski's sign and left ankle clonus That day, the wound was again explored and an extradural abscess found in the region of the squama of the temporal bone and drained She improved until eight days later, when she developed a severe frontal headache, a left facial weakness and Babinski's sign was again present on the left The headache persisted She became stuporous and the pulse dropped from 115 to 60 On January 27, 1937, a lumbar puncture was made The pressure was 150 Mm of fluid, the test for globulin was positive, there were 15 white blood cells, nine of which were polymorphonuclear leukocytes Cultures of the fluid were negative The patient was first seen by me January 29, 1937, 12 days after the onset of the first intracranial symptoms

Physical Examination—The patient was comatose There was no response except to painful stimuli There was a marked left facial weakness The right pupil was

twice the size of the left. The tendon reflexes were active and equal. Babinski's sign was positive on the left. The optic disks were flat and normal. *Diagnosis* Abscess of the right temporal lobe and, although it was thought probably to be a futile procedure, an operation was undertaken.

Operation—January 29, 1937. The first stage was carried out as outlined above. The subdural space was packed off. A needle was inserted. It encountered the abscess at 2 cm, and 45 cc of dirty, reddish purulent material flowed out. Culture showed a hemolytic *Streptococcus*. The wound was closed.

At the beginning of the operation she was comatose, pulse, 60. At the close she was fully conscious and the pulse was 80. Two days later, January 31, 1937, the gauze was withdrawn from the subdural space. Her temperature, pulse and respirations were normal and remained so thereafter. Examination revealed only a left homonymous, upper quadrantic defect in the visual fields and a slight left facial weakness. On February 6, 1937, she complained of a slight frontal headache and 28 cc of pus were aspirated. The following day 20 cc more were removed.

Second Stage—February 8, 1937, ten days after the first stage. The previous incision was reopened. The abscess was now only 1 cm beneath the surface. The abscess was treated exactly as described above. For the next three days the drainage was profuse. By February 16, 1937, eight days after drainage of the abscess, the gauze pack had been removed and the amount of purulent drainage was considerably reduced. Four days later the suture restraining the rubber tube was cut and the tube was gradually extruded, and was entirely removed March 13, 1937, 33 days after drainage of the abscess. The wound was healed by March 24, 1937, and she was discharged from the hospital perfectly well two days later, exactly eight weeks after admission. She was last seen April 25, 1938, at which time she was perfectly well. Neurologic examination was entirely negative and the visual fields were full.

Comment—In addition to strengthening our faith in this method of treatment, this case has made us wary of despairing of any case of brain abscess until all possible therapeutic measures have been exhausted.

Exactly the same procedure is equally suitable for the treatment of abscesses of the cerebellum as illustrated by the following case.

Case 15—Unit No 50693. D. Y., male, age 7, was referred by the Children's Memorial Hospital, Chicago. In the autumn of 1934, he developed pneumonia which was followed by a left otitis media. In February, 1935, an attack of scarlet fever resulted in a reactivation of the otitis media. On March 27, 1935, he developed a frontal headache, continuous vomiting, and as a result rapidly lost weight. He was admitted to the Children's Memorial Hospital two days later. At that time he was alternately irritable and stuporous. There was a slight rigidity of the neck. A lumbar puncture was made. The pressure was "normal." There were 480 white blood cells, 60 per cent lymphocytes. Cultures were negative. There were 56 mg of glucose per 100 cc. He developed a right sixth and seventh cranial nerve weakness, a mild left hemiparesis and became stuporous. Two days later a left external rectus weakness developed. Subsequently his condition improved. Roentgenograms made on April 24, 1935, revealed a slight separation of the cranial sutures. On May 10, 1935, an early papilledema was observed. Eight days later he was admitted to the University of Chicago Clinics.

Physical Examination—There was no spontaneous voluntary movement of the left arm or leg but they were not paralyzed. There was gross incoordination of the left arm and leg with marked flaccidity of those extremities. The gait could not be tested. The optic disks were choked. Ocular movements were full but there was a slow, coarse nystagmus on looking to the left. The tendon reflexes were uniformly diminished.

Babinski's sign was not present. The neck was moderately stiff. Kernig's sign was not present. *Diagnosis* Abscess of the left cerebellar hemisphere.

First Stage—May 23, 1935. The usual incision and small craniectomy were made over the left cerebellar hemisphere. The subdural space was packed about the opening and the wound closed. Two days later he was in excellent condition. The subdural pack was removed.

Second Stage—May 28, 1935. The former incision was reopened. The abscess was found 0.5 cm below the surface. It was opened, evacuated and a firm rubber drain inserted as described above. Smears of the pus revealed *Streptococci*.

Following the operation there was moderate drainage. On June 2, 1935, the suture holding the drain in place was cut and the drain was slowly extruded. It was completely removed June 12, 1935. By June 18, 1935, the wound was healed and the patient was able to walk unaided. He was discharged June 30, 1935, 38 days after the first operation.

When last seen, September 15, 1937, two years and four months after the operation, the boy was perfectly well. There was no evidence of any cerebellar disturbance.

Marsupialization—Occasionally when the wound is reopened at the second operation, the dome of the abscess will be found to have herniated through the defect in the bone (Fig. 1 D). In such cases, the abscess can be opened, evacuated and the capsule sutured to the subcutaneous tissue or scalp, thus marsupializing it as recommended by Hottel.⁶ The abscess is then drained and packed as previously described. In the following case this method was used.

Case 17—Unit No 169671. D. H., male, age 14, was referred by Dr. Raymond Brown of Joliet, Illinois. In November, 1936, he developed an upper respiratory infection. The following month a right otitis media appeared. One week later, December 26, 1936, he developed a severe headache, complained of dizziness and then gradually grew worse. On January 8, 1937, a right mastoidectomy was performed. Although his general condition improved, it was soon noted that the right arm and leg were unsteady. On February 12, 1937, he developed a very severe headache and the following day projectile vomiting appeared. He was admitted to the University of Chicago Clinics February 19, 1937. He was an intelligent cooperative patient. He was and for years had been excessively obese. There was a bilateral papilledema of two diopters. The visual fields were full. Upward conjugate deviation of the eyes was poorly done. There was a nystagmus on looking to either side, more marked to the right, and on looking upward. The right upper and lower extremities were hypotonic and their movements were very ataxic. There was marked dysdiadochokinesis on the right side. He was unable to stand with his feet together and swayed when he stood with his feet wide apart. He staggered when he walked, falling mostly to the left. The neck was stiff. The tendon reflexes were more active on the right. There was a sustained ankle clonus on the right, unsustained on the left side. Babinski's sign was present on the right. The temperature and respirations were normal, pulse, 100. *Diagnosis* Right-sided cerebellar abscess.

Operation—First Stage. February 20, 1937. A vertical incision and an opening in the occipital bone were made over the right cerebellar hemisphere. The subdural space was packed. A needle was inserted which encountered the abscess at 1 cm, 45 cc of greenish white pus flowed out. The organism proved to be a pneumococcus, Type II.

Subsequently his condition was much improved, the ataxia practically disappeared.

The subdural pack was removed in 48 hours, and six days after the first operation the second stage was undertaken

Second Stage—February 26, 1937 The old incision was reopened The dome of the abscess had herniated through the opening in the bone It was incised and the capsule sutured to the subcutaneous tissue The pus within the abscess was evacuated and a firm rubber tube drain inserted

Two days later, he developed a diplopia and a weakness of the right external rectus muscle which persisted until his discharge from the hospital The wound did not drain well On March 7, 1937, nine days after drainage was instituted, the wound became tense and two days later began discharging cerebrospinal fluid The patient was placed flat in bed and fluids were forced The drainage of cerebrospinal fluid was profuse On March 11, 1937, the signs of right cerebellar involvement returned but began to subside about six days later By March 24, 1937, the amount of cerebrospinal fluid drainage had become reduced and four days later it ceased, but herniation of the wound appeared and grew progressively more marked On April 3, 1937, the wound was reopened No abscess was found and the cerebellar hernia was amputated The wound was drained and subsequently discharged cerebrospinal fluid which on culture was found to contain hemolytic *Staphylococcus aureus* On April 19, 1937, the optic disks were flat The patient had no headache There was a marked nystagmus on looking to the right and severe right-sided signs of cerebellar deficit By April 27, 1937, all drainage of cerebrospinal fluid had ceased and the patient was up in a chair A slight purulent discharge persisted On May 13, 1937, a small bony sequestrum was removed By June 9, 1937, the wound was completely healed and the patient was discharged He was able to walk, but rather severe cerebellar signs still persisted When seen November 8, 1937, he had gained 15½ pounds in weight since leaving the hospital and weighed 221½ pounds His station and gait were good He could stand with his feet together without swaying There was still considerable dysdiadokokinesis of the right hand, and his writing, though legible, was poor The wound was well healed, bulging slightly The optic disks were flat He was placed on a limited diet and within a month lost 23½ pounds He is feeling well and the remaining cerebellar signs are rapidly diminishing

Comment—In addition to illustrating the utilization of the marsupialization technic, which is limited in its usefulness to a very small group of cases, this case illustrates the method of dealing with a leak of cerebrospinal fluid employed in this clinic This is a point which will be dealt with in more detail later

Enucleation—Like many other neurosurgeons, we have had the experience of enucleating an encapsulated abscess under the mistaken impression that we were dealing with a tumor Case I was an instance in point It needs no further discussion Vincent's⁸ technic of repeated aspiration of an abscess until it develops a thick capsule and then deliberately reflecting an osteoplastic flap and enucleating the abscess as one would a tumor appeals to us as a rational method of treatment It is most suitable for abscesses in the frontal lobes We have had no opportunity to use exactly this technic since we learned of it but the following case is not dissimilar

Case 10—Unit No 156653 M G, female, age 3, was referred by Dr Frank Greer, Chicago About July 10, 1936, she developed a stye on the left eyelid On July 12, 1936, she fell out of bed striking the region of the left eye The following day she developed a fever of 102° F which persisted for several days On July 16,

1936, a tender swelling appeared in the left temple and the eye was swollen shut. On July 20, 1936, the temporal swelling was incised and pus and blood evacuated. The edema of the eyelids subsided and she was found to have a strabismus. The temporal abscess soon reformed and she was admitted to the University of Chicago Clinics July 29, 1936.

Physical Examination revealed no neurologic or other abnormalities other than the tender fluctuant swelling in the left temporal region. Roentgenograms of the skull were considered normal except for a questionable erosion of the lateral margin of the left orbit. The temporal region was incised and a large abscess found beneath the temporal muscle, which was drained. Cultures of the pus revealed hemolytic *Staphylococcus aureus*. The wound soon healed and the patient was discharged August 26, 1936. On September 3, 1936, she developed nausea and vomiting and was readmitted to the Clinics. Examination revealed a small swelling in the left frontal region just at the hairline. Neurologic and ophthalmoscopic examinations revealed no abnormalities. Roentgenograms of the skull showed a small area of osteomyelitis present beneath the swelling. On reviewing the roentgenograms, made during her previous hospitalization, it was obvious that this area of osteomyelitis, though much smaller, had been present at that time and had been overlooked. The area of osteomyelitis was extirpated and the wound packed. There was no extradural abscess and the dura mater was under no unusual tension. The same organism was cultured. Seven days later, September 15, 1936, she complained of headache and vomited. Examination revealed early papilledema, a diminution in voluntary use of the left arm and leg, a left facial weakness, diminution of the tendon reflexes on the left side with a left Babinski sign. Sensation was intact. *Diagnosis* Brain abscess in the right precentral region (i.e., contralateral to the original infection).

Operation—First Stage. September 16, 1936. The right precentral region was exposed, the subdural space packed. A brain puncture needle was inserted and an abscess encountered at 6 cm. Thirty cubic centimeters of pus were evacuated. Culture revealed hemolytic *Staphylococcus aureus*.

The following day the patient was much better but symptoms of refilling of the abscess soon appeared. Four days after the first stage operation and evacuation of the abscess, a needle was inserted through the wound into the abscess. Pus flowed out, only to be followed shortly by cerebrospinal fluid. This we interpreted as due to rupture of the lateral ventricle into the abscess. At this depth (6 cm) the ventricle presumably lay immediately beneath the abscess. The original needle was replaced by a slightly shorter needle of the T-shaped type designed by Frazier. Within two days the drainage of cerebrospinal fluid ceased and the needle was withdrawn. Her condition continued to improve and it was hoped that repeated aspiration of this deep-seated abscess would suffice, but not so. On October 29, 1936, about one and one-half months after the original aspiration, the wound began to herniate. The abscess was punctured and evacuated repeatedly. The abscess was encountered more and more superficially. On November 17, 1936, the wound was reopened and the opening in the bone enlarged. The subdural space was, therefore, again packed off. A needle encountered the abscess at 3 cm and 25 cc of pus were removed.

Diagnosis—Seven days later, November 24, 1936, the wound was again reopened. The brain tissue overlying the abscess was removed with the Bovie high frequency current. The abscess was opened and evacuated, and beneath it was found a second abscess which communicated with the uppermost by a narrow neck. It, too, was opened, a firm rubber drain inserted, and the cavities packed as previously described.

The packing was removed by December 2, 1936, and the rubber tube by December 21, 1936. The wound soon healed and was depressed. But by January 17, 1937, it was bulging again. Two days later 25 cc of pus were aspirated. On January 22, 1937, 15 cc

were removed January 23, 1937, the wound was again opened. The abscesses were found, evacuated and drained. On February 10, 1937, the drain was finally removed. The wound soon healed and the patient was discharged from the hospital February 14, 1937.

On February 25, 1937, she fell from a chair and struck her head. The next day she developed a headache, vomited and had a temperature of 101.2° F. She was readmitted on February 27, 1937. The wound was bulging and discharging some pus. She had a left hemiparesis which has been present almost from the outset. Thirty cubic centimeters of pus were aspirated but the wound soon filled out again.

Enucleation—March 6, 1937. An osteoplastic flap was reflected. The abscess was carefully dissected free from the surrounding brain but in the inferior part the wall was very thin and ruptured. The ventricle was opened. The wound was drained through the center of the scalp flap, the bone being discarded. Cultures revealed the same organism, namely, hemolytic *Staphylococcus aureus*.

The patient was kept flat in bed. Fluids were forced. A profuse drainage of cerebrospinal fluid continued for two weeks. By April 12, 1937, the wound was entirely healed and has remained so. The child has a severe left hemiparesis but is otherwise well. There have been no further symptoms of recurrence of the abscess.

Comment—In this case both repeated aspiration and drainage failed to cure the abscess. Enucleation was finally undertaken more or less in despair. The results were sudden and excellent. It is unfortunate that the right central region and internal capsule were involved but no method of treatment could have altered this or the appearance of the hemiparesis. This case again illustrates the development and treatment of a leak of cerebrospinal fluid.

Recently, Kahn⁷ has advocated a two stage procedure, at the second stage of which the tumor is enucleated. Kahn's first stage is similar to that described in this paper except that Kahn does not advocate puncturing the abscess—a procedure which, in this clinic, has been found at times to be of great value in reducing the intracranial tension and tiding the patient over to the second stage. At the second stage Kahn has occasionally found the abscess extruded out of the skull. When this occurs, as illustrated by Case 8, abstracted below, the abscess is readily removed (Fig. 1 E). Usually, however, although the abscess will be found to have migrated nearer the surface, it will still be beneath the level of the skull. In such instances Kahn removes the overlying brain tissue by suction, incises and evacuates the abscess and then removes the capsule by dissecting it free from the surrounding brain tissue. It is obvious that removal of an extruded brain abscess *in toto*, when possible, is a highly satisfactory method of treatment. Dissecting the capsule free from the surrounding traumatized and edematous brain tissue after the field has been contaminated by incising and evacuating the abscess is not, however, as free from danger and not a procedure that we have felt justified in employing. The following case illustrates the possibility of removing an abscess after it has been extruded from the skull although the course followed is not identical with that outlined by Kahn.

Case 8—Unit No. 40528. C. B., male, age 19, had been treated in this clinic, where he had been referred by Stanley H. Skrentney, Hammond, Indiana, in June, 1931, because of multiple areas of osteomyelitis. He had suffered from convulsive seizures for years.

About July 15, 1935, he developed an abscess beneath the scalp in the left parietal region. He was admitted to the hospital October 2, 1935, because of this swelling, difficulty in talking and numbness of the right hand. Roentgenograms, revealed an area of osteomyelitis in the left parietal bone.

Physical Examination—The patient had a definite aphasia, the optic disks were not quite clear but were not choked. Sensation was slightly reduced on the right side. The knee and ankle jerks were more active on the right. Babinski's sign was present bilaterally. There was a sustained ankle clonus on the right, unsustained on the left.

Operation—October 3, 1935. The subaponeurotic abscess was evacuated, the area of osteomyelitis measuring 5x6 cm was removed and an extradural abscess 1.5 cm deep at its thickest point evacuated and drained. The infecting organism was *Staphylococcus aureus*.

He rapidly improved thereafter and was discharged October 19, 1935, returning to the outpatient department for dressings. On November 6, 1935, he had a jacksonian convulsive attack involving the right hand. The wound was healed by December 27, 1935. He was quite well until the latter part of January, 1936, when he began to suffer from headaches. On February 26, 1936, the wound was bulging and tense and there was bilateral papilledema of two diopters. He was again admitted to the hospital. There was a slight right facial weakness, the right arm was weak and its movement slow and poorly coordinated. Sensation was slightly reduced on the right. Reflexes in the right lower extremity were increased and Babinski's sign was present.

Operation—February 28, 1936. The old incision was reopened. There was no extradural collection of pus. The dura mater was incised. The brain was brown and gelatinous and adherent to the dura. A needle encountered an abscess a few millimeters below the surface. Subsequent events showed that the abscess should have been enucleated, a procedure which would have been relatively simple. However, because of its location it was incised, evacuated and drained in the hope of causing less neurologic disturbance. There was only moderate drainage. On March 6, 1936, the wound began to bulge. By March 8, 1936, his speech had become worse.

Enucleation—On March 11, 1936, the herniation having become more marked, the wound was reopened. The abscess had herniated out of the skull and was readily removed.

By March 24, 1936, the brain was again herniating, and the patient had become completely aphasic. On April 1, 1936, he had a large infected fungus. Three days later this was amputated with the Bovie electrosurgical unit. A fistula draining cerebrospinal fluid resulted. The patient was placed flat in bed and fluids were forced. The drainage of cerebrospinal fluid continued until April 28, 1936. The wound was healed by June 7, 1936. He has continued well except for a severe right hemiparesis and a partial aphasia.

Comment—The unfortunate permanent result obtained in this case, of a hemiplegia and a partial aphasia, was because of the location of the abscess and is in no way attributable to the method of treatment. Undoubtedly the whole course could have been materially shortened by enucleating the abscess when it was first exposed. That was accomplished in Case 4, where a small abscess, about 3 cm in diameter, was found just beneath the dura and an area of osteomyelitis in the temporal bone.

Repeated Aspiration—Dandy² has recommended that abscess of the brain be treated simply by aspiration. He states that one aspiration may suffice or that occasionally one, two or three additional tapplings may be necessary. Our own experience with this method has not impressed us with its efficacy. In one instance previously cited, Case 10, many more aspirations than four

were undertaken, without more than temporary relief, and much more radical treatment was necessary to obtain a cure. In only one instance was simple aspiration effective.

Case 6—Unit No 90999 J A M, male, age 26, was struck over the head with a lead pipe September 27, 1933. He sustained a compound, comminuted, depressed fracture in the upper right central region. He was admitted to the University of Chicago Clinics about 12 hours after the injury. His left arm was completely paralyzed, the arm was flaccid. There was a left lower facial weakness. The tendon reflexes were diminished in the left arm. He was operated upon immediately. The fragments of bone were removed. One had been driven through the dura. The wound was thoroughly débrided and closed. On October 2, 1933, five days later, purulent drainage (hemolytic *Streptococcus*) appeared. The strength of the arm was improving. The following day the left leg became weak and Babinski's sign was present. On October 10, 1933, a localized subaponeurotic abscess was drained. On October 21, 1933, he had some headache and a moderately stiff neck. The scalp wound was opened more extensively and in doing so the dura was unintentionally nicked. The cortex protruded through this opening. A needle was inserted and at 2 cm encountered an abscess from which several drops of thick pus were obtained. Culture showed hemolytic *Streptococcus*. Only the scalp wound was drained. He soon began to recover and was discharged on November 24, 1933. He has an almost completely paralyzed left arm and walks with a hemiplegic gait, but there have been no signs of progression of his abscess and he has been seen frequently during the years since his accident.

Comment—It seems very questionable whether the aspiration of a few drops of pus from this small abscess played any part in its cure but there was no other specific treatment to which credit could be given.

Leakage of Cerebrospinal Fluid—It has long been felt, in this clinic, that the leakage of cerebrospinal fluid from a wound engenders an unreasonable fear in many surgeons and that it is, therefore, usually treated in a thoroughly illogical manner. This seems particularly true of leakage occurring in association with the drainage of a brain abscess. Obviously, there is but one place for such fluid, infected by reason of its contact with an infected field, and that is outside the skull. To attempt to prevent its escape by closing the opening with devitalized bits of muscle or other means, or by performing lumbar punctures and drawing the contaminated fluid back into the general cerebrospinal fluid circulation, is without merit and only to be condemned as extremely hazardous. Our procedure is to encourage as free a flow of the fluid as possible. To this end, we place the patient flat in bed or even lower the head below the level of the rest of the body and force the patient to take as much fluid as possible. The drainage is allowed to cease and the opening to close spontaneously. This procedure, employed in the six cases which developed such leaks (Nos 8, 10, 12, 14, 16 and 17), has been uniformly successful.

When to Operate—The neurosurgeon has always been greatly concerned about when to operate upon an abscess of the brain. It is generally agreed that operations upon well encapsulated abscesses will be more successful, and that encapsulation requires about four to six weeks. In many instances, however, the patient's condition will not permit of such prolonged delay. An

TABLE
SYNOPSIS OF STATISTICAL DATA RELEVANT

Case No	Name	Unit No	Sex	Age	Date of Onset of Original Infection	Date of Onset of Abscess	Date of First Operation	Date of Discharge	Origin
CERE									
1	W J G	11789	M	15 yrs	11-17-28	12-18-28	5-14-29	6- 7-29	Right ear
2	L K	19702	F	37 yrs	10-15-29	11-14-29	2-13-30	2-22-30	Multiple infections + bloodculture Empyema
3	J P	35919	M	18 mos	8-22-30	(?) 11- 5-30 (?)	11-25-30	Died 12- 5-30 Died	
4	W R	51849	M	61 yrs	4- ?-31	6- ?-31	12-28-31	3- 8-32	Osteomyelitis right fibula and skull
5	R M K	64749	F	3 yrs	3- ?-31	7-10-32	7-28-32	7-29-32	Empyema, bron chiectasis Compound skull fracture ?
6	J A M	90999	M	26 yrs	9-27-33	(?)	10-21-33	Died 11-24-33	
7	M O	106530	F	7 yrs	?	3-14-34	6-28-34	8- 4-34	
8	C B	40528	M	19 yrs	7-15-35	?	2-28-36	6- 7-36	Osteomyelitis of skull
9	V D	154484	F	15 yrs	4-27-36	?	6-28-36	6-30-36	Right ear Died
10	M G	156653	F	3 yrs	7-10-36	9- 3-36	9-16-36	4-12-37	Osteomyelitis of skull
11	I G	168171	F	7 yrs	12-25-36	1-17-37	1-29-37	3-26-37	Right ear
12	T S	178470	M	10 yrs	6-20-37	6-22-37	8-10-37	9-16-37	Right ear
13	N A C	191568	F	6 yrs	11- 1-37	11- 1-37	1-24-38	2-10-38	Ran stick up nose Died into brain
CERE									
14	B S	50693	F	11 mos	1-26-31	3- 1-31	12- 2-31	2- 3-32	Pneumonia
15	D Y	128349	M	7 yrs	Autumn 1934	3-27-35	5-23-35	6-30-35	Left ear
16	G C	153198	F	4 yrs	5- ?-35	5-31-36	6-12-36	4- 5-37	Bilateral mastoid itis
17	D H	169671	M	14 yrs	12-19-36	12-26-36	2-20-37	6- 9-37	Right ear

BRAIN ABSCESS

I TO 17 CASES OF ABSCESS OF THE BRAIN

Organism	Location	Treatment	Cerebro-spinal Fluid Leak	Result	Remarks
<i>BRAU</i>					
<i>Staph aureus</i>	Right temporal	1 stage, enucleation	0	Recovered	Blind before operation
Chest Strep abscess growth	Right parietal	1 stage, drainage	0	Died	No necropsy
<i>Staph aureus</i>	Right parietal	1 stage, drainage	0	Died	Necropsy Multiple (7) abscesses right cerebral hemisphere, meningitis
<i>Staph aureus</i>	Right temporal	1 stage, enucleation	0	Recovered	Died several months later, cerebrovascular accident (?)
Strep	Left occipitoparietal	1 stage, drainage	0	Died	Ruptured into ventricle before operation
<i>Strep hemol</i>	Right central	Single aspiration	0	Recovered	Left hemiparesis, convulsions
<i>Strep hemol</i>	Right central	1 stage, drainage	0	Recovered	Left hemiparesis, Jacksonian convulsions
<i>Staph aureus</i>	Left central	1 stage, drainage later enucleation	+	Recovered	Right hemiparesis, partial aphasia, convulsions years before abscess
<i>Strep hemol</i>	Right temporal	2 stage, drainage	0	Died	Necropsy Abscess removed at second operation, severe edema, meningitis
<i>Staph aureus</i>	Right central	2 stage, repeated aspiration, drainage, enucleation	+	Recovered	Left hemiparesis
<i>Strep hemol</i>	Right temporal	2 stage, drainage	0	Recovered	No sequelae
<i>Strep hemol</i>	Right temporal	1 stage, drainage	+	Recovered	No sequelae
<i>Staph aureus pneumococcus Type XXIV</i>	Right frontal	2 stage, drainage	0	Died	Necropsy Stick found protruding through cribriform plate
<i>BELLAR</i>					
Sterile	Vermis and right hemisphere	1 stage, drainage	+	Recovered	Basilar meningitis spread from this point
Smear Strep culture negative	Left hemisphere	2 stage, drainage	0	Recovered	Impaired vision, retarded growth, obese
<i>Strep hemol</i>	Right hemisphere	2 stage, drainage	+	Recovered	No sequelae
<i>Pneumococcus Type II</i>	Right hemisphere	2 stage, drainage	+	Recovered	Slight cerebellar deficit
			+	Recovered	Slight cerebellar deficit

operation postponed too long may result, if not in death, in blindness (*e g*, Cases 1 and 14). As near as it has been possible to estimate, the period from the onset of the cerebral infection until operation has varied in our cases from 12 days to nine months. In the instance of shortest duration, Case 11, previously cited, the short duration of the abscess infected with hemolytic *Streptococci* cannot be said to have in any way interfered with obtaining an excellent result as this is one of the most striking cases in this series. This patient, whose original infection (otitis media) had occurred only one month previously, and whose first symptom of invasion of the nervous system appeared only 12 days before admission, was brought into the hospital comatose. She was operated upon by the two stage procedure herein outlined, and was discharged from the hospital completely recovered less than two months later.

The majority of abscesses had best be attacked as soon as the diagnosis has been made with reasonable certainty. In a few cases, where conditions will permit, a short delay, with the patient under close observation may be desirable in order to afford more time to allow of better encapsulation. Unfortunately cases where this is possible are all too rare. Not is such delay entirely without danger. Rupture of the abscess into the ventricle (Case 5), the development of a meningitis, or of a severe and fatal cerebral edema (Case 9), are possibilities.

SUMMARY

Seventeen consecutive cases of abscess of the brain treated by surgical means are reported. Twelve of these (70.6 per cent) recovered. Five (29.4 per cent) died. In three of these fatal cases the abscess arose from the lung. In one case, multiple abscesses of the brain were found at necropsy, in another, multiple areas of infection, including the blood stream, were present throughout the body and multiple brain abscesses were suspected, in a third, the abscess had ruptured into the ventricle prior to operation. In the fourth case, the abscess arose from the ear and was located in the temporal lobe, it was a particularly fulminating case and the patient died soon after the first stage. Necropsy revealed that the abscess had been removed at an emergency second operation and that a leptomeningitis was present. In the fifth case, an abscess of the right frontal lobe developed as the result of the penetration of a stick through the cribriform plate into the brain. After drainage of the abscess and relief of the pressure, a basilar meningitis spread backward from the region of the cribriform plate, causing death.

A method of surgical procedure is outlined. It is designed to prevent meningitis by contamination of the meningeal spaces. It consists of two stages. At the first stage, a small craniectomy is made, the subdural space is packed off with gauze soaked in a weak solution of iodine, and the abscess may or may not be punctured and partially evacuated. The gauze is removed 48 hours later. At the second stage, some six days after the first,

the abscess will be found to have migrated nearer the surface. The overlying brain tissue is removed and the abscess is evacuated and drained.

In addition, the questions of enucleation of the abscess, of treatment by repeated aspiration, the problems of dealing with leaks of cerebrospinal fluid, and of when to operate are discussed.

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CARCINOMATOUS METASTASES TO THE BRAIN

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THE treatment of carcinomatous metastases to the brain is a subject which is unlikely to arouse much general interest because of the hopeless outlook from a curative standpoint. However, on the same basis, the ultimate prognosis is almost equally discouraging in infiltrative gliomata (glioblastoma multiforme). In fact, all types of palliative surgery for malignancy fall into this category, in which an eventual mortality is inevitable.

With the realization that curative therapy is impossible, it becomes necessary to seek other criteria upon which to base the advisability or inadvisability of surgical intervention. Obviously, the simplicity or multiplicity of the intracranial lesion is of primary importance. The present report is based entirely upon cases in which the metastasis appeared to be solitary. As in other forms of palliative surgery, three other factors must be considered: (1) The relief of symptoms, (2) duration of life, and (3) the operative mortality. The present cases are analyzed in regard to these three factors.

Giant,¹ in 1926, compared the results in 25 cases, in whom some form of intracranial operation was performed, with those in 22 cases who were not operated upon. He stated: "The average length of life from time of admission to this hospital to death in both verified and unverified cases, whether operated or non-operated, whether radical extirpation or palliative decompression was performed, was less than four months." There is no doubt that these discouraging results have strongly tempered the opinion of the profession regarding surgical intervention in cases of malignant intracranial metastases. However, one conclusion of Giant's is often overlooked. After stating that surgery is unable to prolong the life of these patients, he added: "But surgical intervention for the relief of intracranial pressure is frequently indicated and may go far toward relieving suffering in the last few months of life."

Shelden,² in 1926, reviewed 40 cases of secondary tumors of the brain, from the aspect of diagnosis. Although his paper was not primarily concerned with surgical indications, he distinctly intimated that surgical intervention was not advisable. This passive attitude toward the problem was challenged by Oldberg,³ in 1933. He reported three cases of metastatic cerebral lesions with survival periods of eight months, two years and three years. As further evidence in support of operative intervention, he cited a case of a cervical cord meningioma, wrongly diagnosed as metastatic carcinoma because of previous malignancy. Fortunately, the patient was operated upon and the benign tumor removed. This is a striking example of the fact that

a primary tumor of the central nervous system may occur in a patient with a past history of malignancy. A similar case was reported by Meagher and Eisenhardt,⁴ an intracranial meningioma being removed eight months after a radical mastectomy for carcinoma with axillary metastases.

Concerning the question of symptomatic relief, it is rather difficult to obtain a definite answer from a review of the recent literature, since full case reports are not usually given. However, it is fortunate that we may turn to the experiences of Doctor Cushing,⁵ from whose clinic both Grant's and Oldberg's cases were collected. The statement, "Operations, nevertheless, may not infrequently afford a vast degree of symptomatic relief for which patients and their relatives are most grateful," leaves little doubt regarding the operative relief of symptoms. In addition, he contributes a case of a metastatic carcinoma from the lung with what is probably the longest survival period on record, namely, seven years from the onset of cerebral symptoms and almost six years from the first operation.¹

The factor of operative mortality again necessitates recourse to Doctor Cushing.⁵ Thirty-nine cases were operated upon 50 times with 15 fatalities. The operative mortality of 30 per cent was due largely to the prolonged hospitalization of these patients. It appears likely that this operative mortality has been reflected in the low survival periods reported by Grant.

The evidence just presented could hardly be interpreted as a contraindication to operative attempts upon these unfortunate patients. On the contrary, from the criteria set up at the beginning of this paper, the recent literature must be viewed in a light favorable to surgery. Symptomatic relief, which is perhaps the most important consideration, is specifically noted by both Cushing and Grant. Concerning the duration of life, it must be stated that average survival figures may be misleading by failing to show the extremes of a series. The single case of six years' postoperative life mentioned by Cushing emphasizes the possibility of material prolongation. The operative mortality is not out of proportion to that in glioblastoma multiforme, previously mentioned. Finally, the possibility of disclosing a benign primary tumor must be remembered.

Of secondary interest in the present report is the primary source of the metastases. In the series of 40 intracranial metastatic carcinomata, reported by Meagher and Eisenhardt,⁴ 25 per cent were primary in the breast, 35 per cent were of pulmonary origin and the primary focus was unknown in 25 per cent. The high incidence of origin in the breast and lung naturally raises the converse question of how frequently these specific tumors metastasize to the brain.

Lenz and Fried⁶ found evidence of brain metastases in 21 per cent of 168 cases of fatal breast carcinomata. However, exclusion of those patients in whom skull metastases were likewise present reduced the incidence to 7 per cent. Applying this figure to an estimated five-year-mortality rate of 59 per cent, obtained from the combined figures of Claiborn and Foster,⁷ Cathcart,⁸ McClure and McGraw,⁹ Saltzstein,¹⁰ and Harrington,¹¹ gives a calcu-

lated incidence of about 4 per cent brain metastases without skull involvement from carcinoma of the breast. The composite statistics of Dosquet,¹² Seyforth,¹³ Levy-Simpson,¹⁴ Fried and Buckley,¹⁵ and Davison and Horwitz¹⁶ indicate an occurrence of about 51 per cent brain metastases in cases of primary carcinoma of the lung.

Another question which naturally arises is the relative frequency of solitary and multiple brain metastases. The autopsy series suggest that at least 70 per cent of these metastases are multiple. However, from the symptomatic aspect the proportion is undoubtedly more nearly equal.

Finally, the interval between the appearance of the primary neoplasm and the onset of intracranial symptoms deserves brief consideration. In the breast metastases recorded in Meagher and Eisenhardt's⁴ series, this period varied between the extremes of three months and almost 12 years.

The present report is based upon 14 cases of carcinomatous metastases to the brain, treated by surgical extirpation. The metastatic nature of the lesion was suspected preoperatively in five patients. The malignant character was recognized only after microscopic examination in four cases. The surgical procedures were based upon our established policy for the treatment of primary brain tumors, namely, an extirpation as radical as appears consistent with a satisfactory functional result. Epithelial neoplasms frequently lose many of their malignant characteristics in the foreign environment of the nervous system and assume the appearance of a benign encapsulated lesion. However, necrosis and edema may extend for some distance into the surrounding brain.

CASE REPORTS*

Case 1—J. N., white, male, age 31, was admitted to the hospital October 29, 1929, complaining of headache, and nausea and vomiting, of six weeks' duration. Following in close succession were weakness of the left extremities, retardation of mental processes and generalized weakness. Hospitalization elsewhere, four weeks after onset, revealed slight papilledema, left hemiparesis, right anosmia and mental dulness.

These findings were confirmed on admission to the New Haven Hospital. In addition, there were hyperactive deep reflexes on the left, and inability to sit up. Roentgenograms of the skull were negative. Ventriculography, October 31, 1929, demonstrated what appeared to be a multilocular cystic glioma in the right frontal lobe.

Operation, November 6, 1929, through a right frontal bone flap, revealed a relatively discrete tumor in the superior frontal region. The tumor, about 7 cm. in diameter, was extirpated. Convalescence was uneventful and the metastatic nature of the lesion was not suspected until microscopic sections were studied.

Pathologic Examination †—The characteristic cells were large with pale, foamy cytoplasm and large round nuclei, forming perfect glandular acini. Mitoses were frequent, and extensive necrosis was present in the surrounding brain tissue. *Pathologic Diagnosis*
Adenocarcinoma.

Roentgenologic examination of the chest showed a possible primary carcinoma in the

* General physical examination was negative for signs of malignancy in all cases unless otherwise noted.

† The pathologic examinations and diagnosis in all of the 14 cases reported herewith were made by Dr. H. M. Zimmerman, of the Department of Pathology, Yale University School of Medicine.

upper lobe of the left lung The gastro-intestinal tract was negative for malignancy The patient was discharged November 27, 1929, completely relieved of symptoms

Subsequent Course—Improvement continued for three months, during which time he gained weight and returned to work Death occurred September 29, 1930, almost 11 months after operation

Case 2—H A, white, male, age 63, was admitted to the hospital November 11, 1929, complaining of headache, vomiting and dizziness of four months' duration More recently there had been unsteadiness of gait, transient diplopia, blurring of vision and pain in the left ear Neurologic examination revealed bilateral papilledema, suboccipital tenderness, staggering gait and moderate ataxia of the left arm and leg Roentgenologic examination of the skull was negative

Operation, November 20, 1929, disclosed a discrete tumor in the left cerebellar hemisphere, a grossly complete removal was effected Convalescence was rather slow but essentially uneventful

Pathologic Examination—Microscopically, the tumor presented many irregular glandular alveoli composed of cuboidal, dark staining cells *Pathologic Diagnosis* Adenocarcinoma, possibly prostatic in origin

Subsequent Course—Reexamination of the prostate was negative for malignancy Gastro-intestinal series likewise failed to disclose the primary source of malignancy but roentgenologic examination of the chest showed metastatic involvement of both lungs He was discharged, very much improved, December 20, 1929 Death occurred April 18, 1930, five months after operation

Case 3—A K, white, female, age 52, was admitted to the hospital May 28, 1930, complaining of weakness, vomiting, dizziness, headaches and unsteadiness of four months' duration In 1926 a carcinoma of the right breast was treated elsewhere by simple mastectomy and radium application Axillary metastases were noted in May, 1929, receiving interstitial radium therapy on two occasions

Neurologic examination showed blurring of the optic disks, nystagmus, and left-sided cerebellar signs Roentgenologic examinations of the chest, skull and gastro-intestinal tract were negative for malignancy

Operation, July 7, 1930, disclosed a firm tumor in the left cerebellar hemisphere Subtotal removal of the tumor was followed by a rapid relief of all symptoms

Pathologic Examination demonstrated columns of epithelial cells with abundant mitoses There was considerable necrosis in the adjacent cerebellar tissue

Subsequent Course—She left the hospital July 25, 1930, and remained in excellent condition until about two weeks before her death which occurred in December, 1930, five months after operation

Case 4—M M, white, male, age 52, was admitted to the hospital January 26, 1931, complaining of right temporal headache, blindness of the right eye, difficulty in speech, right facial paralysis, and deafness of the right ear during the preceding ten months In March, 1930, a mass removed from the right cervical region proved to be metastatic carcinoma The positive neurologic findings included involvement of all the cranial nerves on the right, bilateral papilledema, weakness of both external recti and bilateral cervical masses Roentgenologic examinations of the skull and chest were negative

Operation—February 10, 1931 A right subtemporal decompression was effected, and a tumor was partially removed from the region overlying the trigeminal ganglion

Pathologic Examination—Microscopically, the neoplasm was composed of solid cords of large oval cells with vesicular nuclei There were no intercellular bridges or epithelial pearls

Subsequent Course—He was discharged April 5, 1931, somewhat improved, but still complaining of pain in the right trigeminal area This was partially relieved by alcohol injection The patient was readmitted June 9, 1931, because of intractable pain in the right trigeminal field The right trigeminal roots were avulsed through the usual temporal approach, June 10, 1931 Carcinomatous involvement of the roots and ganglion

was demonstrated microscopically. Postoperative roentgenologic examinations of the esophagus and stomach were negative, and he was discharged June 18, 1931, very grateful for the relief of pain.

He was again admitted July 13, 1931, because of pain in the right ear, conjunctivitis and keratitis. Reexamination still failed to reveal the primary source of the carcinoma. The larynx and nasopharynx showed no evidence of malignancy, though in spite of this the latter would appear to have been the most likely primary site. Death occurred October 28, 1931. Considerable symptomatic relief had been obtained over a period of eight months following the first operation, but the patient was never able to resume work.

Case 5—J. B., white, female, age 60, was admitted to the hospital July 2, 1931, complaining of right facial pain for the previous three months. During the last month, headache and diplopia had appeared. Examination disclosed bilateral blurring of the optic disks and involvement of the right fifth and sixth nerves. There was roentgenologic evidence of erosion of the clinoid processes, and the sphenoid sinus.

Operation—July 14, 1931. Exploration of the middle fossa revealed a tumor invading the trigeminal ganglion and floor of the skull and extending through the dura. The trigeminal roots and a portion of the ganglion were avulsed and a partial extirpation carried out on the subdural portion of the tumor.

Pathologic Examination—Microscopically, the neoplasm presented cores of epithelial cells in a dense connective tissue stroma. There were no intercellular bridges or epithelial pearls.

Subsequent Course—Search for a primary focus of the carcinoma was unsuccessful, and the patient was discharged August 10, 1931, completely relieved of headache and trigeminal pain. She died October 27, 1931. The period of satisfactory palliation of symptoms was about three and one-half months.

Case 6—E. B., white, male, age 43, was admitted to the hospital November 9, 1931, complaining of attacks of weakness in the lower extremities followed by severe headache, vomiting, diplopia, transient blindness in the right eye and dizziness of two months' duration. Examination disclosed bilateral anosmia, bilateral papilledema, right sixth nerve paresis, left facial weakness, slight weakness and ataxia of the left upper extremity. Roentgenologic examination of the skull showed a shift of the pineal gland to the left.

Operation—November 14, 1931. Exploration through a right frontal bone flap revealed what appeared to be an olfactory groove meningioma. The tumor and its dural attachment were removed completely and the true nature of the lesion was not suspected until microscopic sections were studied.

Pathologic Examination disclosed sheets of large epithelial cells, with pale, round nuclei, many in mitosis. Occasional acini were lined with tall columnar, ciliated cells containing blepharoplasts. *Pathologic Diagnosis* Carcinoma arising from accessory nasal sinuses.

Subsequent Course—Convalescence was complicated by a nasal, cerebrospinal fluid leak. After a series of roentgen treatments directed at the nasal sinuses, he was discharged December 11, 1931, relieved of symptoms. He died May 15, 1932, six months after operation.

Case 7—L. M., white, female, age 45, was admitted to the hospital August 10, 1932, complaining of headache, vomiting, and dizziness of five months' duration. The significant findings were drowsiness, rigidity of the neck, bilateral papilledema and bilateral sixth nerve paresis. Roentgenologic examinations of the skull and chest were negative. Ventriculography, August 16, 1932, demonstrated an internal hydrocephalus involving the lateral and third ventricles.

Operation—August 18, 1932. Cerebellar exploration disclosed a vascular tumor within the left cerebellar hemisphere having the appearance of a meningioma. The tumor was partially removed.

Pathologic Examination—The tissue was composed of columns of large epithelial

cells, frequently forming small acini, the lumen of which contained pink-staining material resembling the colloid of normal thyroid gland *Pathologic Diagnosis* Adenocarcinoma, metastatic, from the thyroid gland

Subsequent Course—Postoperative examination of the thyroid was negative, but before leaving the hospital a small mass became palpable in the region of the liver. She was discharged September 7, 1932, relieved of her original complaints. She died September 10, 1932, three weeks after operation.

Case 8—M. W., white, female, age 51, was admitted to the hospital November 2, 1933, complaining of convulsions, difficulty in speech, paresthesias in the left upper extremity, headache and vomiting beginning eight months previously. A left radical mastectomy had been performed for carcinoma four and one-half years previously. The positive findings were bilateral papilledema, right sixth nerve paresis, asteriognosis of the left hand. Roentgenograms of the skull were negative.

Operation, November 9, 1933, disclosed a tumor in the right parietal region.

Pathologic Examination—Microscopically, the neoplasm was composed of tall, columnar, epithelial cells forming large, irregular acini. Many mitotic figures were present. *Pathologic Diagnosis* Metastatic adenocarcinoma.

Subsequent Course—The patient was discharged November 29, 1933. She was never able to resume her previous activity, but remained fairly comfortable until her death, January 20, 1934, two months after operation.

Case 9—T. C., white, female, age 45, was admitted to the hospital March 10, 1934, complaining of headache, vomiting and blurring vision of eight months' duration, associated with unsteadiness during the past two weeks. She was operated upon elsewhere in 1928, when a "cancer of the intestine" was removed. Positive findings were bilateral papilledema, left sixth nerve paresis, and cerebellar signs lateralized to the left. There were two lower abdominal scars and a small mass in the left breast which did not have the characteristics of carcinoma. Roentgenologic examinations of the skull and chest were negative for metastases.

Operation, March 12, 1934, disclosed a tumor within the left cerebellar hemisphere. This was completely removed.

Pathologic Examination—Microscopically, the tumor was composed of large cells with hyperchromatic nuclei, arranged in acini and solid columns. Mitotic figures were numerous.

Subsequent Course—The patient was discharged March 24, 1934, relieved of symptoms, and was able to resume many of her household activities until shortly before her death, in December, 1934, nine months after operation.

Case 10—A. S., white, female, age 44, was admitted to the hospital June 4, 1934, complaining of unconsciousness, headaches, vomiting and mental dulness during the preceding eight months. The positive findings were bilateral papilledema, right homonymous lower quadrant anopsia, and the presence of several firm nodes in the left supraclavicular region. Roentgenologic examinations of the skull and chest were negative for malignancy. Ventriculography, June 9, 1934, demonstrated displacement of the ventricular system to the right. The ventricular fluid contained large epithelial cells, sometimes in small groups.

Operation—June 11, 1934. Removal of a left occipitoparietal bone flap disclosed a cyst in the occipital lobe, containing peculiar, pale yellow, milky fluid. A firm nodule was removed from the cyst wall.

Pathologic Examination—Microscopically, the neoplasm was composed of sheets of large cells, some of which had definite polygonal cellular membranes while others appeared to have a syncytial arrangement. The nuclei appeared as large vesicular bodies in an abundant wine-colored cytoplasm.

A lymph node, removed from the left supraclavicular region, June 23, 1934, was diagnosed as squamous cell carcinoma. Roentgenograms of the chest and entire gastrointestinal tract were negative for malignancy.

Subsequent Course—Convalescence was complicated by a thrombophlebitis of the left femoral vein, which delayed her discharge until August 1, 1934. She was able to carry on quite well during her first two months at home. She died December 2, 1934, six months after operation.

Case 11—E. L., white, female, age 59, was admitted to the hospital May 6, 1935, complaining of dizzy spells, loss of memory and interest of seven months' duration. Examination disclosed mental dulness and lethargy, apraxia, slight aphasia and bilateral papilledema. Roentgenograms of the skull were negative.

Operation—Immediately following ventriculography, May 10, 1935, which indicated a lesion in the left frontal lobe, a left frontal bone flap was raised and a tumor removed from beneath the corpus callosum.

Pathologic Examination—Microscopically, the tissue exhibited considerable cellular polymorphism. Many cells were of enormous size with pale, ground glass cytoplasm and huge bizarre hyperchromatic nuclei, in places forming sheets, in other lying singly in extensive pools of hemorrhage. Both mitotic and amitotic division were in evidence.

Pathologic Diagnosis—Metastatic carcinoma, resembling chorio-epithelioma.

Subsequent Course—Pelvic examination and roentgenologic studies of the chest were negative for malignancy. She was discharged May 25, 1935, but was never able to completely regain her normal activity at home, and after several months she became aphasic and confined to bed. She died November 22, 1935, six months after operation. A partial autopsy, limited to the abdomen and performed elsewhere, failed to reveal the primary source of malignancy.

Case 12—J. A., white, female, age 48, was admitted to the hospital December 13, 1936, complaining of headache, vomiting and mental dulness for two weeks. Antedating these symptoms by two weeks, there had occurred a brief attack of syncope during which a scant, fresh rectal hemorrhage occurred. Examination revealed bilateral papilledema, left pupil larger than the right, negative rectal and general physical examination. Roentgenograms of the skull were negative except for minimal evidence of increased intracranial pressure.

Operation, immediately following ventriculography, December 15, 1936, which demonstrated an internal hydrocephalus involving the lateral and third ventricles, a cerebellar exploration, disclosed a tumor within the cerebellar vermis. A subtotal removal of the tumor was accomplished.

Pathologic Examination—Microscopically, the neoplasm presented the picture of a highly malignant cylindrical cell carcinoma, forming acini. Mitoses were frequent, and the cells were arranged in layers around central spaces resembling a carcinoma from the lung or gastro-intestinal tract.

Subsequent Course—This patient did very poorly after operation and was never able to be out of bed. The stools showed a positive guaiac test on two occasions. She was transferred to another hospital, January 7, 1937, where she died January 14, 1937, one month after operation.

Case 13—L. H., white, male, age 47, was admitted to the hospital November 8, 1937, complaining of headache, convulsions, failing memory, olfactory and visual hallucinations of two months' duration. A perforated peptic ulcer had been operated upon 20 years previously, and recurrent episodes of epigastric pain and vomiting had been present during the past ten years. Examination revealed blurring of the optic disks, transient bilateral Babinski and tremor of the hands. Spinal fluid pressure was elevated and the Pandy reaction was four plus. Roentgenograms of the skull were negative. Gastro-intestinal series in another hospital, seven weeks earlier, were reported as negative except for evidence of "adhesions at the pylorus." Ventriculography, November 19, 1937, disclosed xanthochromic fluid in the right lateral ventricle, the third ventricle was displaced to the left.

Operation—December 2, 1937. A cyst in the right frontal lobe was disclosed, which

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contained 40 cc of xanthochromic fluid. A tumor, extending along the wall of the third ventricle, was partially removed, together with the cyst wall.

Subsequent Course—Convalescence was satisfactory until the sixth postoperative day, when drowsiness and fever developed. The bone flap was reelevated and a sizable extradural clot evacuated. During the succeeding week signs of bilateral pulmonary involvement appeared and there was copious "coffee-ground" vomiting on several occasions. Death occurred December 15, 1937, 13 days after operation.

Pathologic Examination—The brain tumor was composed of columnar epithelial cells, forming acini, many of the cells were of the goblet type and mitoses were present.

Autopsy revealed adenocarcinoma of the pylorus with metastases to the left lung, bilateral pneumonia, rupture of the esophagus with gastric contents in the right pleural cavity and right fibrinopurulent pleurisy. The brain contained numerous metastatic lesions varying from microscopic size to 5 cm in diameter and filled (Fig 1) with mucoid material.

Case 14—M. N., white, female, age 34, was admitted to the hospital January 4, 1938, complaining of right-sided weakness and convulsions beginning two months previously. A mass in the left breast, of two years' duration, had been concealed by the patient from her physicians' attention. Examination revealed blurring of the optic disks, right hemiparesis, minimal right hypesthesia, and a firm, fixed mass in left breast with axillary metastases. Roentgenograms of the skull were negative. A film of the chest, however, demonstrated a destructive lesion in the right ninth rib.

Operation, January 6, 1938, disclosed a discrete, subcortical tumor in the left prefrontal region. The tumor was removed in one mass.

Pathologic Examination—Microscopically the sections of the tumor showed it to be composed of columns of poorly differentiated epithelial cells, many of which were in mitosis.

Pathologic Diagnosis Metastatic carcinoma, primary in breast, showing, however, but very little evidence of definite cellular differentiation.

Subsequent Course—The carcinoma of the breast was treated by radium implantation, 7,500 mg h, and she was discharged, February 15, 1938, 40 days after operation. Four weeks later her condition was excellent except for pain in the right arm.

Discussion—Evaluating the preceding cases in the light of the criteria set up at the beginning of this paper, it would appear that operation is not only justifiable but definitely indicated. All cases but two had at least partial relief of symptoms for periods of three weeks to eight months following operation. One-half of them were able to carry on their usual activities. The postoperative survival periods varied from three weeks to 11 months, the average being five months plus. The life expectancy following operation can be best appreciated by reference to Chart 1. The operative mortality for this



FIG 1—Case 13. Cross section of brain showing site of tumor extirpation and several smaller metastatic nodules.

TABLE I
RESUME OF 14 CASES OF CARCINOMATOUS METASTASES TO THE BRAIN

Case No	Sex	Age	Duration of Symptoms	Time in Hospital*	Postoper Survival Period	Period of Symptomatic Relief	Previous History of Carcinoma	Interval between Primary and Secondary	Primary Source		Location of Brain Metastases
									Clinical Impression	Pathologic Impression	
1	M	31	1½ mos	45 days	11 mos	4 mos	None	—	Lung	Kidney or G I tract	Frontal right
2	M	63	4 mos	39 days	5 mos	?	None	—	Unknown	Prostate	Cerebellum left
3	F	52	4 mos	58 days	5 mos	4½ mos	Breast	4 yrs	Breast	Breast	Cerebellum left
4	M	52	10 mos	185 days	8½ mos	5 mos	Metastases to cervical nodes	1 yr	Nasopharynx	Nasopharynx	Temporal right
5	F	60	3 mos	39 days	3½ mos	3½ mos	None	—	Nasopharynx (?)	Nasopharynx	Temporal right
6	M	43	2 mos	33 days	6 mos	6 mos	None	—	Nasal sinuses	Nasal sinuses	Frontal right
7	F	45	5 mos	28 days	3 wks	3 wks	None	—	Unknown	Thyroid	Cerebellum left
8	F	51	8 mos	27 days	2 mos	Never complete	Breast	4½ yrs	Breast	Breast	Parietal right
9	F	45	8 mos	14 days	9 mos	8 mos	Intestine	6 yrs	Colon	G I tract	Cerebellum left
10	F	44	8 mos	62 days	6 mos	3½ mos	None	—	Lung(?)	Lung(?)	Occipital left
11	F	59	7 mos	19 days	6 mos	Never complete	None	—	Unknown	Chono epithelioma	Frontal left
12	F	48	1 mo	25 days	1 mo	0	None	—	Colon	Lung or G I tract	Cerebellum vermis
13	M	47	2 mos	37 days	13 days	0	No Peptic ulcer	—	Unknown	Stomach	Frontal right Multiple in cerebrum
14	F	34	2 mos	42 days	Still living (2 mos)	Still present (2 mos)	Breast	2 yrs	Breast	Breast	Frontal left
Average		48 1	4 7 mos	47 days	5 1 mos plus						

* Includes total time in cases with multiple hospitalizations

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series was 7 per cent. However, it is only fair to state that Case 12 escaped being classified as an operative death only by virtue of the fact that she died in another hospital, to which she was transferred at her family's request. All the other cases were able to return to their homes.

Concerning the primary source of the neoplasms, it is impossible to give an entirely satisfactory answer in four instances (Cases 2, 5, 7 and 11). Three cases (Nos. 3, 8 and 14) gave a previous history of carcinoma of the breast. One patient (Case 9) had an "intestinal" resection for carcinoma, presumably of the colon. Another (Case 4) had nodes of the neck removed for carcinomatous metastases, possibly from the nasopharynx. Finally, one patient

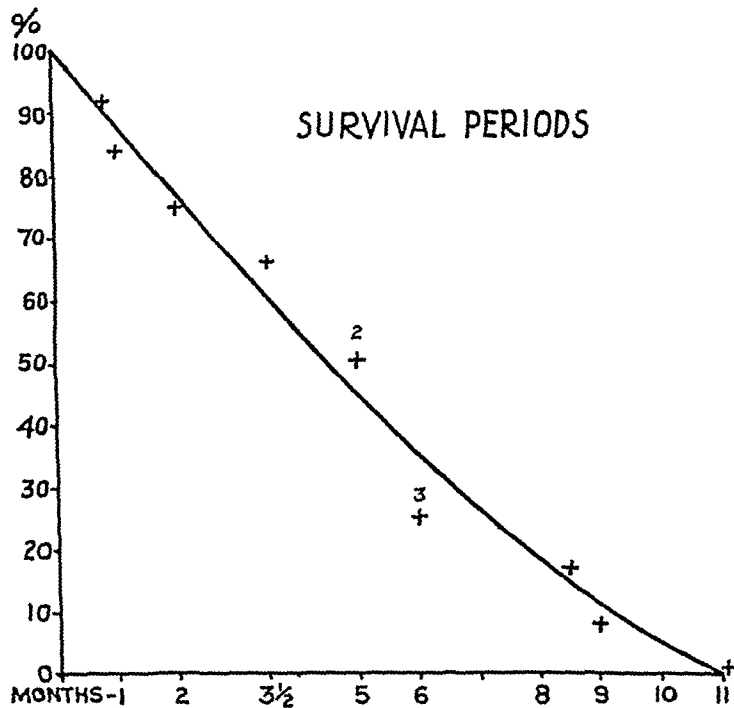


CHART 1—Survival periods of Cases 1 to 12, Case 13 (fatality) and Case 14 (still living) are not included. The numbers "2" and "3" indicate two and three deaths at five and six months, respectively.

(Case 10) had carcinoma metastases verified postoperatively in the supra-clavicular nodes, perhaps secondary to a primary lesion in the lung, which, however, could not be demonstrated roentgenographically. Postoperative attempts to determine source of malignancy were unsuccessful except in Case 1, where a presumptive carcinoma of the lung was revealed roentgenologically. Case 6 obviously arose in the accessory nasal sinuses as evidenced by communication through the cribriform plate and the presence of ciliated epithelium. Case 12 probably had the primary lesion in the colon on the basis of previous bleeding from the rectum and the microscopic appearance of the tumor. The pathologic picture in Case 2 suggested prostatic origin, though this could not be confirmed by digital examination. Similarly, the thyroid was implicated in Case 7 but palpation failed to reveal any abnormality.

However, these two sites—prostate and thyroid—are known to harbor small areas of carcinoma which may give rise to early metastases. It is perhaps pertinent in this connection that both patients had extensive metastases elsewhere—both lungs in Case 2 and the liver in Case 7. The nasopharynx is suggested as the primary site in Case 5 because of the clinical and pathologic similarity to Case 4. Autopsy confirmation in Case 13 revealed a carcinoma of the stomach with multiple metastases to the lung and brain. Finally, the tumor in Case 11 resembled a chorio-epithelioma, though pelvic examination and partial autopsy failed to confirm this. In the four cases with a history of previous primary malignancy, the intervals preceding admission for brain metastases were two, four, four and one-half and six years.

Certain other facts of interest are illustrated in Table I. In this series females outnumbered males nine to five. The average age was 48.1 with extremes of 31 and 63. The distribution by age decades is shown in Table II.

TABLE II
DISTRIBUTION BY AGE DECADES

Decade	4th	5th	6th	7th
Patients	2	6	4	2

Regarding the location of the brain metastases, it is somewhat surprising to find the cerebellum involved in five cases in spite of its relatively small size. All lobes of the cerebrum were represented, the frontal in four cases. The only peculiarity of lateralization was the fact that the right cerebral hemisphere was involved more often than the left (5/3), while the right cerebellar hemisphere was never implicated (0/4, 1 in vermis). Multiple metastases in both cerebral hemispheres were found at autopsy in one case.

Finally, consideration of the period of hospitalization is of some importance. The average was 47 days with extremes of 14 and 185¹. This latter figure included three separate hospitalizations ending in a long terminal illness because the patient could not be cared for adequately at home. However, even excepting this unusual instance, there was too much time spent in the hospital, both before and after operation. Reference to Chart 1 illustrates that the life expectancy at best is in the neighborhood of one year and that 50 per cent of these patients will probably be dead within six months. Further, their period of greatest usefulness is likely to be shortly after operation. With these economic factors in mind, it does not seem justifiable to prolong hospitalization in the hope of locating the primary site, since curative therapy is out of the question. This is further emphasized by the fact that such studies revealed the primary focus in only one case of this series. If general physical examination and roentgenologic studies of the chest are negative, it is probably wiser to concentrate on an attempt to obtain a postmortem examination when death occurs.

SUMMARY AND CONCLUSIONS

Fourteen cases of metastatic carcinoma of the brain are reviewed and analyzed in respect to operative results. The period of symptomatic relief varied from zero to eight months, one-half of the patients were able to resume their usual activities. The postoperative survival periods varied from three weeks to 11 months, with an average of five months plus. The operative mortality was 7 per cent.

The probable primary sources of the neoplasms were: Breast, three, lung, two, colon, two, nasopharynx, two, prostate, one, thyroid, one, accessory nasal sinuses, one, stomach, one, and chorio-epithelioma (?), one.

The distribution of patients in respect to sex was females nine, males five. The average age was 48.1 with extremes of 31 and 63.

The metastases were located in the cerebrum in nine instances and the cerebellum in five. One case had multiple cerebral metastases.

The period of hospitalization averaged 47 days with extremes of 14 and 185. It is suggested that every attempt be made to shorten this period because of the limited life expectancy.

The conclusion is drawn that operation is definitely indicated in patients with metastatic carcinoma of the brain if the metastases are apparently solitary.

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EPIDURAL SPINAL INFECTIONS *

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DANDY,¹ in 1926, collected 25 cases of epidural abscess from the literature, and added three cases of inflammatory tumors (one tuberculous) to seven previously reported. Five of these were probably of syphilitic or tuberculous origin. The largest group of epidural abscesses personally observed, was published by Mixer and Smithwick,² in 1932, who reported 10 cases. Browder and Meyers,³ in 1937, reported on seven patients, five of whom had abscesses and two inflammatory tumors. This article contains a very complete bibliography and a tabulation of 88 cases, which include both the acute abscesses and the granulomata, and represents all cases recorded from 1855 to 1937, indicating the comparative infrequency of such infections. In the present communication we wish to report seven cases, five of acute epidural suppuration and two of granulomata. Neither tuberculous nor syphilitic infections are under discussion.

Etiology—There may be some question of the advisability of considering the more or less chronic granulomata with the acute abscesses. They seem, however, to other observers and to me, to have a common etiology. Infections of the epidural space are considered to occur by direct spread from contiguous structures or by metastasis from a distant focus. When there is a direct invasion from a neighboring infected structure, such as a vertebra or rib, the mechanism is readily understood and is not debatable. In the larger group, which is more important and more difficult to diagnose, the infection arises as a metastasis from a distant lesion, such as a furuncle or an infection of a finger, which may have healed and been forgotten before the onset of the spinal symptoms. Many observers have felt that in most instances the metastatic infection is to the epidural spinal fat. Browder and Meyers hold with some others that the hematogenous variety most likely always metastasizes to the vertebra whence it spreads into the epidural space. The evidence they present is very suggestive, especially the postmortem findings of vertebral involvement. As they correctly observe, a small area of osteomyelitis might readily be overlooked at operation. Where there is as extensive a bone lesion as is described by these authors, there is every probability that the epidural space was involved secondarily. It is, however, possible for the vertebra to be invaded from without. The microscopic study of the bone removed in Case 4, suggested this spread, though it does not, of course, rule out an overlooked primary focus in a neighboring vertebra. The stump of a lamina in Browder and Meyers' Case 7 was probably secondarily invaded.

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Pathology—Once involved, whether from a metastasis to the epidural fat or by spread from a vertebra, the lesion in the epidural space is made up of a varying amount of free pus and granulation tissue. The pus may be large in amount and extend from the cervical to the lumbar region, and there may be no granulation tissue. On the other hand, the granuloma may be the only evidence of a chronic infection. There may or may not be droplets of pus in it, or the combination of considerable granulation tissue and a large amount of free pus may exist. The inflammatory tumors, chronic granulomata, are found beneath the site of a previous skin infection or of trauma to the back. Where there is free pus only, the dura is reddened though it preserves very often its normal luster. Where granulations exist they are attached to the dura, on its dorsal and lateral aspects. In the acute cases this attachment is not as intimate as is found in the granulomata where sharp dissection is necessary to free the dura. The fact that there is an actual space between the vertebra and the dura dorsally, allows the pus to spread upward and downward, while the dura itself acts as an effective barrier to the invasion of the subarachnoid space. On the anterior aspect, however, as other observers have pointed out, the dura is intimately attached to the posterior bodies of the vertebra. A large extradural collection of pus is not encountered and perforation into the subarachnoid space is more frequent.

The seriousness of the disease is the damage done to the spinal cord. In the few cases where careful histologic studies of the cord have been reported (Ayer and Viets,⁴ and Hassin⁵), the changes noted have been out of proportion to the pressure of the abscess. There have been noted areas of rarefaction, vacuoles, destruction of fiber tracts and cells. Elsberg⁶ explains the findings on the basis of local interference with the circulation of blood in the cord. Browder and Meyers state, in Case 3, "Many blood vessels of the cord were thrombosed, being filled with septic thrombi."

Symptoms—In the acute cases the history given by the patients is very uniform and the course of the disease varies but little and that only in its time elements. The onset is marked by pain in the back. The site of the pain varies with the location of the lesion. If in the rare instance of a process in the cervical region, the pain will be in the back of the neck, radiating up to the occiput and down into the arms, if low in the thoracolumbar spine the pain will be low in the back with early radiation down the legs. The most frequent site is in the interscapular region, or a little lower, with radiation around to the anterior part of the chest or upper abdomen. The pain should not be referred to just as pain and passed over, it is probably one of the most excruciating pains in the back that a patient can have. It is more or less constantly present and seemingly ever increasing in severity. It is not relieved by the recumbent posture. In fact, many of these patients cannot lie down. Morphine hardly seems to control the agony.

During this period the temperature is usually elevated, but its degree varies considerably. It may reach 103° to 104° F or not go above

100° to 101° F. In from a few days to about two weeks, neurologic signs make their appearance. While the most frequent early complaint is tingling or numbness in the legs, weakness in the legs or bladder disturbances may be the first sign. The rapidity with which the paralysis progresses varies. It may go on to a complete flaccid paraplegia within a few hours (almost minutes) after the onset, or it may take several days to reach this stage. During this time there will be a weakness gradually increasing in one leg, then involvement of the other. In fact, patients have been reported with a flaccid paralysis of one leg and a spastic paresis of the other. In a very few cases the motor changes may be limited to a foot drop, to a weakness of one leg or to spastic paresis of both legs. But the rule is for a rapid progression to the stage of flaccid paraplegia.

An analysis of the time of onset of the neurologic signs from the beginning of pain in the back was possible in 49 reported cases of metastatic abscesses. In 14 cases the interval was five days or less, in 19 cases the first neurologic sign appeared between the sixth and tenth day, in 10 cases between the eleventh and fifteenth day, and in six cases it was over 15 days. The very short interval in some cases indicates the primary invasion of the epidural space and prompt interference with the vascular supply of the cord.

The sensory findings are not as constant as the motor, though most often there will be found loss of all sensation below the level. There are, however, cases in which the motor signs are much more marked than the sensory. At times the sensory level will be found to extend upward from day to day. Early loss of sphincteric control is common. Tenderness over the spine at the site of the lesion is a constant finding.

Two additional observations are of help in arriving at a diagnosis. The white blood count is elevated, with an increase in the polymorphonuclear cells. Lumbar puncture yields further information. If a manometric determination is made, there will be block on jugular compression. The fluid is often xanthochromic, though it may be clear. The total protein content is high and there may be, though not necessarily so, a pleocytosis.

More than a word of caution is needed in advocating lumbar puncture. Regardless of the site of origin in the canal of the infection, many patients will have pus in the epidural lumbar space because of a gravity abscess. This was encountered in three of the five patients in the present series. There exists, then, the obvious danger of traversing the layer of pus and infecting the subarachnoid space, initiating a meningitis. If the diagnosis be suspected, the stylet should be removed from the needle after the skin has been traversed. In this way pus would be obtained before the dura is reached.

In the granulomata the evolution is less rapid and more closely resembles that of cord compression from a tumor. The pain, while less than in the abscess cases, is much more severe than that seen in spinal cord tumors except some of the giant tumors of the cauda equina.

EPIDURAL SPINAL INFECTIONS

CASE REPORTS

Case 1—Barnett Hospital, Paterson, N J, No 31274 P F, male, age 16, was admitted to hospital August 24, 1930. On August 18, 1930, a superficial abscess had been incised over the knee. Twenty-four hours later he developed pain in the lower abdomen and chest. Two days later the neck became painful and was held rigidly. The temperature on admission was 104.2° F. The neck was rigid and a positive Kernig sign was noted. W B C, 42,000, polymorphonuclears, 90 per cent. The spinal fluid contained one cell and what appeared to be Cocci. Though the culture was negative, anti-meningococcus serum was given. Culture of fluid, obtained the following day, was also negative. On August 26, no fluid was obtained on two attempts. The following day a few drops of pus were obtained from the lumen of the needle introduced into the lumbar region and clear fluid with 17 cells from the cisterna. There was weakness of the legs, tenderness and fulness over the upper thoracic spine, and roentgenologic evidence of bone destruction of the arch of the fourth thoracic spine. Laminectomy revealed an abscess in the soft parts, disease of the fourth spinal arch and free pus in the epidural space. The culture yielded *Staphylococcus aureus*. The patient did not improve following this drainage. He was unable to void, though no new neurologic signs appeared. On September 3, drainage of the lumbar epidural space was instituted by laminectomy. A blood culture, on September 5, yielded *Staphylococcus aureus* in pure culture. The patient died on September 7, 1930.

This type of epidural abscess was secondary to an osteomyelitis of the vertebra, but was only part of a picture of a general sepsis. In the light of further experience the necessity of the second laminectomy is questionable, although when it was carried out considerable undrained pus was observed in the lumbar epidural space.

Case 2 *—Mount Sinai Hospital No 348583 G L, male, age 6 months, was admitted to the Pediatric Service, February 1, 1933, because of fever for six days. The temperature range was from 99° to 103° F. On the day of admission rigidity of the neck was noted. This and a questionable injection of the pharynx were the only abnormal physical findings at the time of admission. A lumbar tap the following day yielded xanthochromic fluid which contained 150 cells. W B C, 15,200, polymorphonuclears, 46 per cent. Three days later the spinal tap was repeated. At this time only a few drops of xanthochromic fluid were obtained which showed 160 cells, of which 70 per cent were polymorphonuclear in type. On the eighth day after admission, a flaccid paralysis of both upper extremities appeared. Two days later, a spastic paralysis of the lower extremities occurred. About this time, a swelling was noted to the right of the lumbar vertebrae (neurosurgical consultation was requested). Pus was obtained from the epidural region in the third lumbar space, and pressure over the swelling increased the flow from the puncture needle. It was felt that this pus represented a gravity abscess from a lesion originating in the cervical region. However, roentgenologic examination of the cervical spine disclosed no abnormality. An immediate operation was undertaken.

Operation—The pus in the lumbar musculature was found to communicate with the epidural space in the region of the second lumbar vertebra. The spines and laminae of lumbar II and III were removed and pus was seen in the epidural space pouring down from above. A long drainage tube (subsequently shown roentgenologically, to reach the first thoracic vertebra) was inserted epidurally and the wound packed, wide open. A culture of the pus was reported to contain an hemolytic *Streptococcus*. Improvement in motor power began six hours after operation and continued until there was normal power.

* This case was reported by L W Rauh in the Journal of the Mount Sinai Hospital, 1, 13, 1934.

in all extremities. Lipiodol was injected into the tube to determine, if possible, the site of the cervical lesion. It reached the seventh cervical vertebra, but nothing abnormal was seen here. The drainage tube was removed six days after the operation. The boy was seen three and one-half years later and appeared normal.

The origin of this epidural abscess was never determined. All we know is that it probably arose in the cervical and extended to the lumbar region. The surgical procedure, while unorthodox, that is, drainage in the lumbar region, seemed to us to be following the path nature pointed out. In any event, in this instance it was satisfactory. The finding of an hemolytic *Streptococcus* is somewhat unusual, the majority of such abscesses are due to a *Staphylococcus*.

The cervical region is least often involved. Of 50 collected cases of metastatic abscess, only four were in this region.

Case 3—Mount Sinai Hospital No 390090. R. M., female, age 15, was admitted to the hospital, because of a paraplegia of one day's duration, with an antecedent history of boils of the face and a more recent history of severe back pain. A complete transverse lesion at the tenth thoracic segment was found. Laminectomy disclosed an epidural spinal abscess. No return of function.

During the month prior to the onset of her present illness, she had had many boils of the face. Two weeks before admission she began to have pain in the lower part of the back. At first, she continued at school, but the pain kept increasing in severity so that finally she was unable to lie in bed and found most comfort in the standing position. The morning prior to admission there was a rapid onset of paraplegia and loss of ability to void. Fever had not been noted, and at the time of admission the temperature was 99.6° F. Examination showed a flaccid paraplegia with loss of all sensation and reflexes below the tenth thoracic segment. W. B. C., 20,000, polymorphonuclears, 80 per cent. A spinal tap yielded faintly xanthochromic fluid containing 37 leukocytes, a total protein of 135 mg per cent, and complete block on manometric determination. A laminectomy was undertaken within an hour after admission. The spines and laminae of thoracic VI and X were removed. A thick layer of granulation tissue covered the posterior dura, in addition there were about 10 cc of free, thick pus, from which a *Staphylococcus aureus* was cultured. The patient was discharged 65 days postoperative, without any return of function.

Case 4—Mount Sinai Hospital No 398729. G. K., male, age 23, was admitted to the hospital, because of pain in the back and fever for three days. Under observation, meningeal signs appeared. Laminectomy revealed an epidural abscess in the lower thoracic region. Recovery.

As a boy this patient had suffered with osteomyelitis of many of the long bones and had had an osteoarthritis of the hip. He had been well, however, for eight years, until two months prior to his present illness, when he began to suffer with furuncles over the body. Some of these, as well as recent scars, were present when he entered the hospital. Three days prior to his admission he began to complain of pain in the lower back, which increased in severity and was associated with fever. A severe headache developed three hours before admission, at which time he had a temperature of 102° F. There was tenderness over the twelfth thoracic spine as well as in the left costovertebral angle. The neck was held rigid, a bilateral Kernig sign was present, and a zone of hyperesthesia was noted over the eleventh and twelfth thoracic dermatomes. W. B. C., 16,900, 86 per cent polymorphonuclear cells. On admission two diagnoses were considered—a perinephric abscess and an osteomyelitis of the spine. The following morning the signs remained unchanged. A lumbar tap was considered inadvisable, therefore a cisterna tap was performed, which yielded cloudy fluid containing 2,000 cells with 60 per cent poly-

morphonuclear leukocytes, but no organisms on spread and subsequent culture. An immediate laminectomy from thoracic XI to lumbar I was carried out. This disclosed pus overlying the dura with little granulation tissue. The operative exposure seemed to reach the limits of the infection. The wound was packed wide open. Although the meningeal signs persisted a few days, convalescence was smooth for three weeks, when signs of an abscess in the soft parts of the thigh appeared. This was opened a week later, and the patient went on to a complete recovery. The pus from the epidural space showed *Staphylococcus* on culture.

Pathologic Examination—Dr Paul Klemperer. Specimen. Bone removed at the time of the laminectomy. "There is a very severe, acute purulent inflammation with actual abscess formation on the surface of the endosteal fascia of some of the particles. One can see a purulent inflammatory reaction within the haversian channels. Within the bone marrow one can also see in places very conspicuous purulent inflammation and an increase of polymorphonuclear leukocytes is notable throughout. However, there is no evident bone destruction in the interior of the particles."

"In view of the fact that there is actual abscess formation on the surface, one can hardly understand that the bone would not be severely destroyed, in at least some areas, if this surface reaction would be an extension of the process from the bone to the surface. For this reason I feel certain that one must conclude that the osteomyelitis is secondary to the inflammation on the surface."

In this instance, we were fortunate to have a very early case, before the onset of any neurologic signs other than meningeal irritation. He was operated upon 16 hours after he entered the hospital, just four days from the onset of the back pain. This is the earliest diagnosis and operation that we have found recorded. The case reported by Slaughter, Fremont-Smith and Munro⁷ was operated upon five days after the onset, after 66 hours of observation.

Case 5—Mount Sinai Hospital No 401224. S. P., male, age 26, was admitted to the hospital with an 11-day history of back pain and a one-day history of weakness of the legs. Immediate laminectomy was performed for drainage of an epidural spinal abscess. Spread of the infection to the anterior mediastinum which was drained one month later. Death.

Three weeks before the onset of pain in the back an infected finger had been incised. The back pain was noted on arising one morning, 11 days before admission to the hospital. The day before admission there was loss of power in the legs and inability to void. During this period he claimed to have been afebrile, on coming to the hospital his temperature was only 99.4° F. He looked sick. There was percussion tenderness over the fourth to sixth thoracic spines. Very slight power remained at the hips and the left knee. There was a sensory level at the seventh thoracic segment below which sensation was diminished. The deep reflexes were still present in the legs and a Babinski sign was found on the right. The neck was slightly rigid and a bilateral Kernig was noted.

A lumbar puncture was carefully performed, the stylet being withdrawn before the dura was penetrated. Slightly xanthochromic fluid was obtained which showed a complete block to jugular compression. There were 30 cells, and the total protein was 90 mg per cent.

Laminectomy of thoracic IV, V, and VI disclosed a large amount of free pus, under pressure, in the epidural space. The dura was covered with a thick layer of granulation tissue. The wound was packed wide open. The pus showed *Staphylococcus albus* on culture.

During the next few days power began to return in the legs, and sensation improved. Ten days after operation the temperature began to rise. At first no cause could be found

Later retention of pus was noted in the wound. At a second operation this was found to come from beneath a rib and subsequent roentgenologic examinations showed a pre-vertebral abscess. This was drained on the Thoracic Service, but the patient succumbed five days later. Postmortem examination revealed multiple pulmonary abscesses and bronchopneumonia.

Cases 6 and 7 illustrate types of inflammatory tumors or chronic granulomata.

Case 6—Beth David Hospital No 30-1972 J K, male, age 65, was admitted to the hospital August 26, 1930, with the history of having been in an automobile accident in February, 1930. The patient had no recollection of a direct blow to the spine though he recalled having been badly shaken up. Four months later, he began to complain of pain in the lower back, which was intensified on coughing or sneezing. For six weeks before his admission, he had noted weakness of the legs, which increased so that he was confined to bed. For four weeks he had difficulty in voiding. When first seen in consultation, September 12, 1930, he had almost complete paraplegia with spontaneous flexion contractions. The deep reflexes in the legs were increased and a bilateral Babinski response could be obtained. The sensory level was about the tenth thoracic segment. The thoracic vertebrae, VIII and IX, were sensitive to pressure. Lumbar puncture demonstrated a complete block.

Operation—September 13, 1930. Laminectomy disclosed, beneath the thoracic vertebrae VIII and IX, a dense mass of tissue encircling the dura on its dorsal and lateral aspects. This could not be separated from the dura bluntly. It was split in the midline and parts removed by sharp dissection. The pathologic report of the excised mass, verified by Dr. Joseph H. Globus, was chronic granuloma. There was considerable post-operative improvement, so that the patient was able to get around and he could control his sphincter.

The appearance on the operating table was that of an extradural sarcoma, however, it was more dense and adherent than is usually the case in that type of tumor. The very clear-cut traumatic history must be considered as a possible etiologic factor even in the absence of evidence or history of a direct blow.

Case 7—Mount Sinai Hospital No 409313 S W, male, age 44, was readmitted to the general surgical service, three and one-half months after he had been discharged following an operation for a carbuncle of the neck. The infecting organism was a *Staphylococcus aureus*. He had a mild diabetes, which could be readily controlled by dietary regimen. Shortly after he left the hospital he began to complain of pain in the back of the neck which radiated up to the occiput. Flexion and lateral motion of the head and neck were limited by pain. About two weeks before his readmission the pain had become aggravated.

On examination, it was noted that flexion of the neck caused shock-like pains in the legs. The power in the right arm was diminished. The deep reflexes in the lower extremities were increased, the right more than the left, and a Babinski response was obtained on the right. Tenderness was present over the spine of cervical two and three, and an indefinite sensory level seemed to be present at the second cervical segment. The following day the weakness of the right arm had increased. Some weakness appeared in the left arm, and there was retention of urine. A lumbar puncture showed a block, and the fluid contained 104 mg of total protein. W B C, 13,500, 86 per cent polymorphonuclear cells.

A preoperative diagnosis of granuloma was made, which was verified by laminectomy.

The mass lay on the dorsal and lateral aspects of the dura beneath the cervical vertebrae I, II and III, and was rather readily peeled off the dura. A lumbar tap, performed nine days after operation, demonstrated that there was no longer any block.

Pathologic Examination—Dr Paul Klemperer: "Sections of the material submitted show dense, almost hyaline, connective tissue, one fragment showing an area of calcification. The veins and capillaries are engorged with blood. There is perivascular infiltration with lymphocytes and occasional polymorphonuclear leukocytes and plasma cells extending here and there into the adjacent connective tissue. Connective tissue fragments showing chronic inflammation. No evidence of phlebitis."

Diagnosis—At the onset, in the acute abscess cases, the pain in the back, the initiating symptom, will give no lead as to the actual condition. Such a pain, associated with a mild or even a high temperature, can be, of course, due to any one of a number of conditions. As the pain continues, however, with ever-increasing severity, a suspicion as to the possible underlying pathology will be aroused. If the history of antecedent infection is obtained, and the pain is as low as the lumbar region, associated with some tenderness over the muscles in that region, a perinephric abscess may be suspected, as it was in Case 4. With the advent of paresis, poliomyelitis will be thought of. In this condition, however, one does not find sensory changes. After the advent of the paralysis, a spinal cord tumor will be considered. The finding of xanthochromic fluid and block may further suggest this diagnosis. However, increased temperature, if present, the leukocytosis, and the rapidity of the progression of the motor signs speak against the usual spinal cord neoplasm. If, as is often found, the paraplegia is a flaccid one, we have additional evidence. While a similarly rapid progression, associated with a flaccid paraplegia, is sometimes seen in spinal cord tumors, they will usually be found to be the result of a metastasis. The age-group in most cases of acute epidural spinal abscess is against this possibility.

In the chronic granulomata a history of an overlying infection may suggest the pathology of the lesion, as it did in Case 7. While a history of a direct trauma would bring up the same question, in most instances the diagnosis of spinal cord tumor will be made and the pathology will be disclosed only at operation.

Treatment—There is only one treatment for acute, epidural spinal abscess—prompt operation. A laminectomy, to provide adequate drainage of the infected focus, should be performed, and the wound left wide open. In most cases the removal of the arches from two or three vertebrae will be sufficient. In rare instances a more extensive procedure, or a second laminectomy in the lumbar region, may prove necessary. In Case 2, lumbar drainage was adequate in caring for a cervical lesion. In the chronic granulomata the indications and treatment are those of spinal cord tumor.

Prognosis—As far as can be determined from reported cases, no instance of epidural spinal abscess has lived unless operated upon. The outcome of operation can be considered from two aspects, one, as to life, the other, as to return of function. If the sepsis continues actively, so that the intraspinal abscess is only a part of the picture, the prognosis is that of the sepsis. This

was surely the condition in Case 1 and probably in Case 5. Another possibility, also shown in Case 5, is the spread of the infection, even though it was considered adequately drained at the time of the primary operation. A third factor leading to a fatal issue is that found in all cases of complete transverse lesions of the cord. I refer to the respiratory and urinary tract infections and spreading decubitus.

Meningitis, as a complication, is relatively rare when the dorsal epidural space is involved. The dura offers a real barrier to the spread of the infection to the subarachnoid space. In the rare instances, where the lesion is anteriorly placed, meningitis seems to be more frequent.

Functional return will depend on the extent of the damage to the spinal cord before treatment is instituted. In the face of a flaccid paraplegia, such as was seen in Case 3, no improvement can be expected. If, fortunately, the diagnosis is made early, as in Case 4, the functional result will be perfect. In between these two extremes there are any number of gradations.

SUMMARY

The relationship of acute, metastatic epidural abscess and chronic granulomata of the epidural space is discussed.

Five cases of abscess and two of granuloma are recorded. Their symptomatology and diagnosis are discussed. The need of prompt recognition and adequate surgical treatment, especially in the abscess cases, is emphasized.

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TOXIC MYELOPATHY (SPINOCAINE)⁴

SOME CONTRAINDICATIONS TO SPINOCAINE ANESTHESIA

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NEUROLOGIC complications following spinal anesthesia have been reported frequently. It is the purpose of this communication to review some of the literature, report four cases, and consider the pathology of toxic myelopathy.

The use of spinal anesthesia has become widespread except in instances of severe myocardia disease, hypertension, marked hypotension, and psychoneuroses. The following exceptions to the employment of spinocaine should be added. Congenital anomalies in general, particularly those of the central nervous system, and diseases of that system, congenital anomalies and diseases of the circulatory system, such as tendency to, or presence of, varicosities, endarteritis or phlebitis, and congenital anomalies and diseases of the skin and epidermal appendages, such as pilonidal cyst (Case 2), with which spina bifida occulta is often associated. These exceptions are made to direct attention to conditions which are inherent and are early evident, those which may appear late, and those which may be early acquired. These include affections of neural structures, and disturbances of the circulation of those structures. A diminished vascular efficiency would not favor immediate, and possibly even delayed, restitution of function of a spinal cord bathed by toxic cocaine derivatives.

Stovaine¹ (amylococaine hydrochloride) injected into the subarachnoid space of dogs and apes causes degeneration of the roots and periphery of the cord, and retrograde changes in the anterior horn cells. The spinal anesthetics² commonly employed (nupercaine, spinocaine, gravocaine and seurocaine, which contain procaine as their chief constituent) have been shown to be both myelolytic and hemolytic. When injected into dogs they produce an aseptic meningeal reaction with an exudation of plasma cells and a proliferation of arachnoidal cells, which later results in a thickening of the meninges, disintegration of axones and degeneration of the peripheral portion of the cord. Somewhat similar changes have been demonstrated³ in the spinal cords and nerve roots of patients dying following spinal anesthesia (procaine hydrochloride).

Following the subarachnoid injection of 5 per cent procaine hydrochloride into rabbits,⁴ the reversible reaction was followed for 24 hours. At two hours

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there were chromatolysis and swelling of the cells, with scarcely any normal cells in the anterior horns. At six hours there was much improvement and at 24 hours the cells were normal again. Unfortunately this does not always occur, nor is it known why, except that the conditions mentioned above might be considered as predisposing to such complications.

In addition to the effects of the anesthetic, an error in technic might be a factor. When the spinal needle is inserted, it is important that further progress of the needle be arrested just after it has passed through the dura. Pushing the needle further may traumatize the closely matted nerves of the cauda equina and the vessels of these nerves. An admixture of blood may change the properties of the injected anesthetic and lead to a reactive fibrosis in the form of leptomeningeal adhesions. Still further progress of the needle will bring it to the anterior wall of the spinal canal which often contains a large emissary vein from the body of the vertebra. The impact of the needle against the bone, and the pain of which the patient complains, indicate that the needle has reached that point. A sharp shooting pain down one leg or a sudden flexion of that leg would indicate that one of the nerves of the cauda equina had been irritated. Conservatism might dictate that the mishaps mentioned be considered as contraindications to continuing with the spinocaine anesthesia.

As an anesthetic, spinal has about the same immediate mortality, and death rate from postoperative pneumonia, as has ether, but is superior to it in that it produces greater muscular relaxation and does not have the ill-effects which follow ether.

Foss and Schwalm⁵ have reported 3,000 cases of spinal anesthesia (procaine hydrochloride) without a single neurologic complication. Others⁶ have reported percentages of 0.01 (procaine mainly, as well as stovaine and spinocaine and others) to 0.5 (compilation of 2,074 cases in which spinocaine, neocaine and novocaine were used).⁷ Almost any part of the central nervous system may be affected, with the involvement remaining permanent or causing a fatality. Hyslop⁷ divided the neural complications into three types: (1) Local or neighborhood, such as lesions of the cauda equina, (2) distant focal, such as cranial nerve palsies, (3) general, such as aseptic meningitis or meningo-encephalitis.

Block⁸ reported seven cases with a pathologic study of one. Case 1 (procaine preparation) was an acute, benign, lymphocytic meningitis with a high spinal fluid sugar; Case 2 (nupercaine) a severe meningitis characterized by polynucleosis and disappearance of sugar from the spinal fluid; Case 3 (procaine preparation) an almost fatal polio-encephalitis with residual 19 months later; Case 4 (procaine preparation) a severe radiculitis involving the area of the groin, scrotum and testicles and appearing three weeks after the anesthetic; Case 5 (nupercaine) severe cauda equina neuritis 24 hours after a second spinal, the first one having been given 37 days previously; Case 6 (type of spinal anesthetic not stated) a cauda equina neuritis with mild cord involvement which in the next 29 months developed into a fatal transverse

myelitis and radiculitis. Immediately on injecting the spinal anesthetic the patient suffered such severe pain radiating down the legs that a general anesthesia had to be employed in order to complete the operation. Case 7 (nupercaine) developed a toxic myelopathy with the symptoms of spinal shock and a fatal issue in three months. Examination of the spinal cord in this case revealed extensive destruction of the myelin sheaths, axis cylinders and glia, mostly at the periphery of the cord and at the entrance zones of the posterior roots. The ganglion cells of the anterior and lateral horns were also slightly involved. Davison and Keschner,⁹ in their study of toxic myelopathy (toxins from bodily infections), noted that the periphery of the cord, being closest to the toxic substance, was more involved than the central parts, and that there was a lack of glial response, which is consistent with a disease of short duration. Davison and Keschner^{10 11 12 13, 14} have clarified the problem of spinal cord disease and emphasized the extreme rarity of true myelitis of infectious origin. They preferred to call all other cord affections myelopathies due to toxins or circulatory interference.

It was Brock's⁸ belief that all the neural complications could not be explained on the chemotoxic effect of cocaine derivatives, but assumed that there must be a tissue sensitivity. In Case 4 there was a long interval between the anesthesia and the onset of symptoms, and in Case 6 a cauda equina neuritis and a mild cord involvement progressed to a fatal transverse myelitis. "One is led to assume that an original chemotoxic effect permitted other factors (virus?) to operate on a neural tissue devitalized by the anesthetic." A polyneucleosis with a disappearance of sugar in one spinal fluid and a lymphocytosis in the other strongly suggests the presence of a virus in one of them.

CASE REPORTS

Case 1—A male, age 21, was admitted to the hospital July 4, 1932. A pilonidal cyst was removed without sequelae, 15 cc of spinocaine was used. A recurrence was excised, in July, 1934, under spinocaine anesthesia, 15 cc being used. In January, 1935, a second recurrence was removed under 15 cc of spinocaine. The diagnosis was infected dermoid cyst containing a nest of hair. Varicose veins, which had appeared in both lower limbs since his second admission, were successfully injected. In April, 1935, a third recurrence, containing sebum and hair, was excised under 15 cc of spinocaine. The cyst never extended deeper than the fascia over the coccyx.

Immediately following the last operation, he complained of numbness of the right lower quadrant of the abdomen, perineum, penis, the right buttock, thigh and the whole right leg, flaccid paralysis of the right leg, urinary retention and bowel incontinence. At first he required catheterization but later could evacuate the bladder by suprapubic pressure. Bowel incontinence or constipation remained. He had no control over enemata. On discharge, two and one-half months after the last operation, his bowel and bladder control had not improved. His leg, however, had begun to recover function, though it was still numb and stiff.

He had his fifth admission October 13, 1936, because of bowel and bladder difficulty. It had required five months before he could walk upstairs and the same period before sufficient anal sphincteric tone developed to prevent fecal incontinence. It took him 30 to 45 minutes to expel a two quart enema. In October, 1935, his older brother, age 29, had a pilonidal cyst successfully removed under ether anesthesia.

Physical Examination—Showed well healed wound at site of pilonidal cyst removal, right testicle atrophic, no sensation to firm pressure or rubbing in any part of the rectum reached by the inserted finger, mucosa above internal sphincter redundant and relaxed, moderate mucosal prolapse on straining in the squatting position, a few small external rectal tags, internal sphincter tone fair, external sphincter tone poor. Over the left lumbar area, arranged like the petals of a sunflower, were café-au-lait spots covering an area the size of a man's hand. The old, rather prominent injected varicosities could be seen and felt on the left knee and the right calf.

Neurologic Examination—Patient right-handed, walked slightly favoring the right leg, on which balancing was fair as compared to the left, gluteal reflex fair on the left, poor on the right, absent right knee jerk, ankle jerk and semitendinosus reflex, slight paresis of all flexors and extensors in the right leg as compared to the left, with tonus and mass of the right buttock much diminished, anesthesia, thermesthesia and analgesia from the third to the fifth sacral segments on the right. Cramal nerves negative.

Laboratory Data—Urine negative. Blood and spinal fluid Wassermann negative. Spinal fluid and manometric readings normal. Roentgenologic examination of the lumbosacral spine showed no evidence of any abnormality of the spine. The right sacro-iliac joint showed moderately increased density due to a mild osteo-arthritis. There was no evidence of spina bifida occulta.

Cystometrogram—Revealed a bladder of normal capacity but slightly increased irritability, a tendency to develop desire to void, and pain at low normal pressure and capacity, with very rapid response to pilocarpine causing early desire to void and pain mainly on volitional bladder evacuation. The bladder had been previously infected.

Subsequent Course—Various parasympathomimetic drugs were used for therapeutic and diagnostic reasons as well as combinations of these with laxatives and pituitrin. The most favorable combination consisted of 4 cc of fluid extract of cascara sagrada and 8 cc of mineral oil at 9 00 P M, and after breakfast, at 8 00 A M, $\frac{1}{2}$ cc of surgical pituitrin subcutaneously. Within five minutes he had a complete and satisfactory bowel and bladder evacuation. At 10 00 A M, and 3 00 A M, he took orally 1/16 gr of pilocarpine and had two complete bladder evacuations.

Second Cystometrogram—February 3, 1937. Revealed a less irritable bladder, with desire to void and pain at the average normal pressures, and an ability to develop intracystic pressure on straining to void with help of the abdominal muscles, almost twice what it had been before. This indicated a definite increase in control over the voluntary muscle and an even more marked and rapid response to pilocarpine greater than normal.

Neurologic Examination—February 4, 1937. Still gets cramps in the posterior muscle group of the right leg on exertion. Absent right knee jerk and semitendinosus reflex with return of ankle jerk. Left upper extremity reflexes more active than lower, with left abdominals more active than the right. Both cremasterics absent. Right buttock still flabbier than the left but firmer than previously. The weakness in the right leg was limited to flexion at the knee. Slight hypalgesia in the third and fourth sacral segments with a patch in the fourth lumbar segment. Much more and diffuse pressure sensation in the lower bowel except in the midline posteriorly under the operative scar. Mucosa not as redundant as previously. *Clinical Diagnosis*—Toxic myelopathy (spino-caine).

COMMENT—The recurrence of a pilonidal cyst is not uncommon. The successful administration of spinocaine anesthesia three times would hardly seem to raise a question about a fourth except that recurrently subjecting the spinal cord to a toxic substance might merit consideration, especially when the fourth was relatively soon after the third, namely, four months. It is known, however, that procaine hydrochloride spinal anesthesia has been administered five times in 38 hours,¹⁵ and spinocaine 14 times in 17 months.¹⁶

without injuring the spinal cord. The development of varicose veins between the second and third admissions and the finding for the first time of hair in the pilonidal cyst indicated the development of latent anomalies, one quite close to the end of the spinal cord and both possibly reflected in the coverings or substance of that structure. The finding of hair and sebum in the cyst the fourth time further affirms the progressive development of ectodermal dysplasias. Varicosities may be due to an inherent defect in the vessel walls and when they are associated with varicosities of the spinal cord, the vascular efficiency of that structure is impaired.

The café-au-lait spot had not changed but had always been present as an evidence of another ectodermal dysplasia. The occurrence of a pilonidal cyst in an older brother is also of interest. However, it indicates that an anomaly which may be familial, though not hereditary in this case, appears earlier and is more developed in those born later. This patient, ten years younger than his older brother, developed a pilonidal cyst at age 18 while it did not appear until the latter was age 29.

Whether the osteo-arthritis of the right sacro-iliac joint was present before the toxic myelopathy cannot be said, but it is unlikely. The atrophic testicle was not. It is possible that both these conditions are the result of a disease of the trophic centers for these structures in the spinal cord or at least for testicular innervation. The inordinate bladder response to pilocarpine without a comparable general reaction is suggestive. The relaxation of the muscles and tendons about the right sacro-iliac joint could have exaggerated the normal stresses and strains to traumatic importance.

Case 2—A male, age 39, was admitted to the hospital September 25, 1936, with the diagnosis of postoperative appendiceal hernia and right indirect inguinal hernia. On January 1, 1936, and again two months later, he had been operated upon for a ruptured appendix. He had worked for two months in the interim.

Physical Examination on admission was negative, except that he was a very tense, apprehensive, overconscientious, and a somewhat suspicious individual.

Laboratory Data—Urine, blood Wassermann and Kahn reactions negative.

Operative Procedure—September 28, 1936. Both herniae were repaired. Three cubic centimeters of spinocaine were employed. Just before operation the patient's blood pressure was 178/78. After operation, as on admission, it was 120/80. The next morning the patient could void but complained of excruciating shooting pains in the left hip and calf and to a less extent in the right calf. On the third day he felt better but had tingling sensations in both legs. On the fifth day he insisted his legs felt paralyzed although he seemed to move them normally. On the fifteenth day he had developed pain and tenderness in the left heel. On the twenty-second day he was up and about but complained of pain in the perineum, drawing sensation in the left groin, some disturbance in anal sphincteric control, and at times terrific pain deep under the operative wound, radiating through to the back. Repeated urine examinations were negative.

Neurologic Examination—October 26, 1936, 28 days postoperative. The patient stated that if he walked upstairs too frequently he developed a spasm in the perineum. No penile erection had been experienced since operation, and there was no spontaneous desire to void or defecate. He had "no control about emptying the bowel," and noted that if he "took a deep breath" it would evacuate spontaneously.

The patient walked very carefully, with his legs apart as if straddling a painful peirneum of which he actually complained. Balancing poor on the left foot, tremor of the extended fingers, right more than left, which the patient stated had been present before operation, deep tendon reflexes were increased with the left biceps greater than the right, left knee jerk greater than the right, but right ankle jerk greater than the left, hypalgesia and thermhypesthesia from the third to the fifth sacral segments bilaterally. The external anal sphincter was weak and the internal sphincter gripped the finger poorly. As far as the rectal examining finger could reach there was no sensation of pain and only on the left lateral wall was there a slight feeling of pressure to very firm palpitation by the inserted finger.

Cranial Nerves—Right pupil greater than left, with both reacting well to light and accommodation, vision 20/15 in both eyes, both ocular fundi were quite hyperemic, with all the vessels engorged, optic disk margin on the left was indistinct, suggesting pseudoneuritis. The smaller arteries showed diffuse and irregular narrowing.

Cystometrogram—October 28, 1936. Normal bladder oscillations, first desire to void felt at 350 cc with pressure of 120 Mm of water, pain felt at 600 cc with pressure of 270 Mm, with straining could reach only 270 Mm, following the injection of pilocarpine grains $\frac{1}{8}$, with the bladder containing 350 cc, after 30 minutes, the pressure was only 180 Mm.

Spinal Puncture—November 3, 1936. Fluid clear and colorless, no increase of cells or globulin. Initial pressure was 160 Mm of water, and the manometric readings were normal. The patient insisted that many of his symptoms disappeared following this procedure and subsequently urged when they recurred that it be repeated.

Using parasympathicomimetic drugs, the patient's bladder and bowel control improved markedly, and on December 18, 1936, a cystometrogram revealed normal findings.

Neurologic Examination—December 18, 1936. The patient had been able to walk four or five miles daily. Deep reflexes in left upper extremities were increased and right ankle jerk was greater than left, normal plantar responses. Slight hypalgesia over the third and fourth sacral segments on the right, and over the upper end of the third sacral segment on the left.

The patient's tenseness and anxiety had become less, but his hypochondriacal preoccupation, with many bizarre variations of his initial complaints, became marked. In spite of every reassurance that he had recovered, he refused to believe this, and had to be discharged against his wishes January 4, 1937. *Clinical Impression*—Toxic myelopathy (spinocaine), and cauda equina neuropathy, psychasthenia.

COMMENT—A very neurotic male, age 39, with premature senility, had, after prolonged illness which had an additional unfavorable effect on his already hypochondriacal attitude, a repair of two herniae under spinocaine anesthesia. Subsequent to this he immediately complained of pain down his right leg and developed signs and symptoms of a cauda equina neuropathy, from which he recovered almost entirely as shown by neurologic examination and cystometrogams. However, his mental attitude became definitely worse. It would seem that because of his neurotic make-up, premature graying of his hair and early cerebral vascular changes, he was a poor risk for the administration of spinocaine anesthesia. The poor recovery he made from the toxic effects of the drug, and the mental reaction that he exhibited, once this had occurred, seemed to substantiate this.

The inadvisability of administering spinocaine anesthesia to a patient who is very tense, anxious and agitated before an operation, as well as fearful of

it, must be emphasized. Three cases of postoperative atelectasis and pneumonia following spinocaine anesthesia have been observed. Panic on the part of these patients seemed to be a very important factor. They hold themselves rigidly, not only because of mental perturbation but also from fear of pain. Their respirations are extremely shallow, resulting in a minimal movement of the diaphragm and little aeration of the lower lobes of the lungs, with consequent poor blood oxygenation which predisposes to atelectasis. This occurs in cases where no permanent injury remains to the spinal cord. These individuals also exhibit a predilection for hysterical conversion symptoms of a motor or sensory nature. Affections of bowel, bladder and potentia also occur. All of these are most disturbing not only medically but also from a forensic point of view.

Case 3—A male, age 60, was admitted to the hospital December 2, 1936, because of external and internal hemorrhoids. For 25 years he had been "extremely nervous."

Physical Examination—A well developed well nourished white haired very tense male. Blood pressure 120/80. Peripheral vessels moderately thickened, and tortuous. Dorsalis pedis pulses present. Internal and external hemorrhoids with dilation and tortuosity of hemorrhoidal veins.

Laboratory Data—Urine and blood Wassermann negative. Spinal fluid and manometric readings normal.

Operative Procedure—December 4, 1936. The hemorrhoids were injected with 8 cc of 5 per cent phenol in oil, under 60 mg of spinocaine anesthesia. Immediately after operation he could move his legs but the left one had a "restless feeling." The urinary stream was weak and the stools thin and unformed. On the second day the right arm began to shake, and he had a shooting pain behind the right ear on turning to the left, the pain in his right index finger was so severe he could not close his fist.

Neurologic Examination—December 12, 1936. The right arm hung limply at the side, on walking forward with his eyes closed, he wandered ataxically to the left, ataxic intention tremor bilaterally on finger to nose test, very slow in performing fine finger movements with the right hand, left dysidiadokokinesis, gross rest-tremor of the right upper arm which extended to the hand on attention, intention and excitement, right hyper-reflexia with all deep reflexes being generally increased, abdominal reflexes diminished, but the cremasteric reflexes very active, right grip weak, left lower leg deformed and somewhat atrophied due to an old fracture but with good power, vibratory sensation diminished in all toes, more so on the left.

Cranial Nerves—Both pupils of almost pin point size, the left being slightly greater than the right. Both reacted promptly, though to a very limited degree, to light and accommodation. Smaller retinal arteries showed slight narrowing.

Following a spinal puncture, the tremor of the right upper arm disappeared temporarily.

Cystoscopic Examination—December 23, 1936. Right, left and middle lobes of prostate markedly enlarged. Median bar markedly hypertrophied. Marked trabeculation of the bladder wall. Contracture of the bladder. Re-examination, February 23, 1937, revealed that normal bowel and bladder function had been restored. The right arm still swung slightly less than the left. Moderate fine tremor of the extended fingers bilaterally, right more than left, reflexes all equally hyperactive, motor power good throughout except for old left leg weakness, no sensory disturbances, pupils unchanged. He was discharged to duty March 4, 1937.

Clinical Diagnosis—Toxic myelopathy and radiculopathy (spinocaine), generalized arteriosclerosis, psychasthenia.

COMMENT—The long history of nervousness, the presence of peripheral, cerebral and very likely spinal cord vascular sclerosis, varicosities of hemorrhoidal veins and pupillary anomalies suggesting central nervous system involvement, seemed to have made this patient a poor candidate for spinocaine anesthesia. He developed signs and symptoms suggesting involvement of the spinal cord and radicular nerves as well as paresis and tremors of a functional nature. His recovery was fairly rapid and almost complete although there were still some slight residua on discharge.

Case 4—A male, age 28, was admitted to the hospital September 25, 1932, because of right lower quadrant pain which had started 12 hours previously.

He was much wrought up, feeling that due to general mismanagement his life had been endangered. He became even more convinced of this upon the unhappy progress of his case.

Physical Examination—Well developed, tall, athletic male who appeared acutely ill. Blood pressure 110/68. Heart and lungs negative. Right lower quadrant tenderness and spasm.

Laboratory Data—White blood count 12,800, P-78, L-14, M-8.

Operative Procedures—An appendectomy was performed the day after admission. During the spinocaine anesthesia (2.4 cc), there was much respiratory embarrassment and irregularity of the pulse. Immediately after the operation the patient complained of pain and weakness in the left leg and pain in the right ankle. He also began to vomit. This continued, in addition to having attacks of tachycardia with a pulse of 180 and no comparable temperature rise. On September 30, 1932, under gas-ether anesthesia, an exploratory celiotomy and an entero-enterostomy were performed. Generalized peritonitis and a constriction at the ileocecal junction were noted. Following a stormy convalescence his intra-abdominal condition improved.

Neurologic Examination—November 4, 1932. Hypesthesia of the entire left leg except for the area between the toes and the inner side of the arch. This was felt to be of a functional nature. He was discharged, improved, November 7, 1932.

On December 2, 1932, he was readmitted because of stiffness of the tendons and aching pains in the left leg, particularly of the ankle which became swollen on exercise. At times he could not walk because of this discomfort.

Neurologic Examination—December 8, 1932. On Lasèque maneuver the patient complained of pain in the popliteal space. The circumference of the left calf was 1 cm less than the right. Some urinary frequency during the day but no incontinence. Hypalgesia in area on anterior aspect of the thigh corresponding roughly to the intermediate cutaneous and medial cutaneous branches of the femoral nerve, though not of as great extent. It was felt that the spinocaine anesthesia was not the cause of these findings. Roentgenologic examination, December 10, 1932, revealed only slight soft tissue swelling in the posterior of the right ankle joint due to a mild synovitis.

He also complained of recurring violent abdominal cramps. Barium studies revealed the hepatic flexure to be slightly displaced to the left on account of a large liver. The transverse colon showed a spastic state, with the midtransverse colon constantly located in the right lower quadrant, suggesting adhesions.

Third Operation—December 28, 1932. Under spinocaine anesthesia (2.2 cc), the adhesions causing the obstruction were severed. The entero-enterostomy was functioning. The patient again had a stormy convalescence, and developed a right, non-specific epididymitis and orchitis, and attacks of tachycardia of sudden onset and cessation, reaching at times approximately 200 systoles per minute. Electrocardiogram in the free interval was negative. He was discharged, improved, February 1, 1933. During the next four years he had five hospital admissions for symptoms relating to the sequelae of the spinal anesthesia.

At the time of his eighth admission (March 17, 1937, to May 10, 1937), he had developed, in addition to pain in both knees and ankles, pain in the left shoulder, elbow and wrist

Three weeks after admission he was transferred to the Neurologic Section where he was observed for two weeks. He had remissions and exacerbations without apparent cause. The ache was deep in the joints, not in the bone or surrounding tissues, which was not aggravated by motion or pressure but was made worse by effort and fatigue so that he became "wobbly." He was irritable and dissatisfied.

Neurologic Examination—April 15, 1937. Gait was normal, on Romberg he swayed mostly to the left and backward (he felt he was turning counterclockwise and to the left), when eyes were closed and extended arms were brought to horizontal, the body and arms turned to the left. Balancing on each foot was fair, poorer on the left foot, pass points to the right with the left hand. Area of hypesthesia ("feels like roughness and itching you want to scratch"), hypalgesia ("like burning") and hypthermesthesia in the second and third lumbar segments on the anterior aspect of the left thigh. Calves were of equal size and the left thigh 1 cm greater than the right (ref examination December, 1932, at which time the left calf was 1 cm less than the right).

Psychotherapy was begun with considerable enthusiasm on the part of the patient. Since the operation, in 1932, he had had marked insomnia, restlessness, easy fatigue, constipation and increasing disinterest in his work. He had married happily, December, 1936. Since childhood he had had nightmares. A review of his life history and attitudes revealed the origin of some of his character traits to him. He always had a feeling of inferiority and felt that no one was interested in him. With this attitude he abandoned himself to all manner of escapades, always submitting to punishment without question when caught.

Even with the most superficial explanations of his problems he greatly improved, and all the above symptoms disappeared. On the day of his discharge back to duty, the only neurologic signs were sensory disturbances in the second and third lumbar segments on the left thigh, characterized by hypesthesia, with a feeling of dulness, hypalgesia, with a burning quality, and hypthermesthesia. *Clinical Diagnosis*—Toxic cauda equina neuropathy (spinocaine), traumatic neurosis (improved).

COMMENTS—An athletic, previously healthy male had an appendectomy, performed under spinocaine anesthesia. Following this a whole train of unhappy symptoms developed and resulted in eight hospitalizations. His upper respiratory infection favored the employment of such an anesthetic, but his extremely wrought-up mental condition should have precluded its use. How much his mental state played a part in initiating his vomiting attacks and perpetuating an already confused situation, ending in two additional operations, can only be problematic.

In reviewing his case with him, he constantly emphasized what he believed to be gross mismanagement as the causative factor. He had developed signs and symptoms of a toxic neuropathy affecting the cauda equina, peritonitis, intestinal obstruction, polyarthritis and traumatic neurosis in addition to his own character neurosis.

The motor as well as the sensory portions of the nerves were affected as indicated by the increase in size of the left thigh and calf in 1937, as compared with the measurements in 1932. It is possible that recovery might have been retarded by the second spinocaine anesthesia and the perpetuation of the dysesthesiae¹⁷ which were so distressing, favored. The importance of the

patient's mental attitude in exaggerating symptoms which had a real organic basis and developing others as a functional elaboration must be mentioned. That this was the case was substantiated by the change in the picture following psychotherapy.

SUMMARY

The literature on neural complications following spinocaine and other forms of spinal anesthesia is reviewed to emphasize their frequency and unpredictability.

In addition to excluding patients having severe myocardial damage, hypertension or marked hypotension, other exceptions to spinocaine have been added. These are congenital anomalies in general, particularly those of the central nervous system and diseases of that system, congenital anomalies and diseases of the circulatory system, such as tendency to, or presence of, varicosities, endarteritis or phlebitis, and congenital anomalies and diseases of the skin and epidermal appendages, indicating possible disease of the central nervous system, such as pilonidal cyst. The importance of severe neurotic traits as a contraindication to the employment of spinocaine anesthesia was emphasized.

The first case reported was that of a young male who, following his fourth spinocaine anesthesia, developed signs of a severe spinal cord and cauda equina neuropathy from which he never fully recovered. The recurring pilonidal cyst, developing varicosities in the lower extremities and cafe-au-lait spots, were suggested as possible contraindications to repeated spinocaine anesthesia.

The second case was that of a male, age 39, with presenility and severe hypochondriasis, who developed signs of a transient cauda equina neuropathy from which he recovered, but in whom a residual, severe psychesthesia developed, which was built up about the symptoms resulting from the original neural lesion.

The third case was that of an adult male with generalized arteriosclerosis, varicosities of hemorrhoidal veins, pupillary pathology and a long history of "nervousness." Following spinocaine anesthesia he developed signs and symptoms of an organic and functional nature indicating diffuse spinal cord and radicular nerve pathology, from which, however, he made a gradual recovery but of which there were still some residuals.

The fourth case was that of a very healthy, athletic male, age 28, whose appendix was removed under spinocaine anesthesia, during a period in which the patient was in a much wrought-up mental condition. He developed signs and symptoms of a cauda equina neuropathy, an intestinal obstruction, which required two subsequent operations, and a traumatic neurosis resulting in eight subsequent hospitalizations during the following five years. The atrophy of the left leg had disappeared but the dysesthesiae have remained. Much improvement in all his symptoms followed psychotherapy.

It is suggested that if the above criteria for the selection of cases are considered, the number of complications following spinocaine anesthesia would be diminished.

Addendum—Since this report was submitted for publication, a fifth case has been observed four years after spinocaine anesthesia. There was evidence of a severe myelodradiculopathy of the lumbar spinal cord and nerves. Marked vasomotor instability was noted, the signs and symptoms of which were known to have been present even before the spinal anesthetic was administered. Such vascular disturbances have been suggested as contraindications.

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THE EFFECT OF BREATHING 95 PER CENT OXYGEN UPON THE INTRALUMINAL PRESSURE OCCASIONED BY GASE- OUS DISTENTION OF THE OBSTRUCTED SMALL INTESTINE

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IN A NUMBER of recent communications the value of breathing 95 per cent oxygen for the relief of intractable gaseous distention of the intestine has been set forth on the basis of clinical and experimental data^{1 2 3 4}. The laboratory studies which provided the basis for clinical application of the method demonstrated the capacity of 95 per cent oxygen to deflate a closed loop of small intestine distended with nitrogen, which, in man, forms the major constituent of the distending gases. The mechanism by which the oxygen accomplishes this result consists in the exclusion of nitrogen from the inspired air. According to the law of gases, the diffusion of any gas through a semi-permeable membrane is proportional to the difference between its partial pressure upon the two sides of the membrane. Inhalation of pure oxygen necessarily reduces the pressure of nitrogen in the lungs toward zero, so that nitrogen in the blood diffuses into the expired air, and by the same mechanism the resulting reduced partial pressure of nitrogen in the blood allows this gas to diffuse more rapidly from any body cavity or tissue space into the blood, whence it is expelled through the lungs. *The oxygen per se has no direct effect on the diffusion process. Its virtue lies only in the fact that, when properly used, it is a convenient respirable gas which prevents nitrogen from being inhaled.*

The experimental studies clearly demonstrated that. By causing an animal to breathe pure oxygen instead of air, the volume of nitrogen in a closed loop of small intestine distended with this gas can be reduced in 24 hours to about 40 per cent of its original volume. This is in contrast to an average variation of only 10 per cent of the original gas volume when the animal breathes room air for the same period of time. The pathologic changes in ileus are primarily referable to the effect of increased intraluminal tension, rather than gas volume. We propose, therefore, in this paper to supplement the observations already published^{1 2 3 4} on gas volume changes with experimental data on comparative intra-intestinal pressure changes in the bowel distended with air or nitrogen. (1) In animals breathing room air, and (2) in animals breathing pure oxygen.

Method—The abdomen of cats, starved for 24 hours, was opened under intraperitoneal nembutal anesthesia and the pylorus ligated. A large glass

cannula was securely tied into the lowest portion of the ileum and an occluding ligature placed immediately distal to the cannula. The abdominal wall was closed around the other end of the cannula, which was connected by a T-tube to a mercury manometer and to a Perusse pressure bottle. The intestine was then inflated with atmospheric air by increasing increments of pressure until a final pressure of 800 Mm of water was established at the end of five hours. This pressure was maintained for one hour, following which the Perusse bottle was clamped off. The intraluminal pressure was recorded on a slowly moving kymograph until the animal died or was sacrificed. One group of 12 cats breathed atmospheric air, another group of 14 breathed pure oxygen from the time the Perusse bottle was clamped off until the experiment terminated. Intra-intestinal pressure tracings, data on the bowel and peritoneal fluid content, bowel weight, length, and gross appearance were compared in these two groups. A third group of four cats, in which the intestine was similarly treated except that no air was injected into the intestine, served as controls for the data on bowel weight and length, intra-intestinal and intraperitoneal fluid content. All of the animals were kept under intraperitoneal nembutal anesthesia for the duration of the experiments.

The selection of a final intra-intestinal pressure of 800 Mm of water (60 Mm Hg) as a basis for a comparison of the deflating process in an animal breathing air as against one breathing oxygen, is somewhat arbitrary. It was chosen because it represents a level of intraluminal tension which, though considerably in excess of that which is ordinarily observed clinically,* may, if sustained for a number of hours, be considered sufficiently high to cause local and constitutional effects and at the same time to serve as an adequate test of the capacity of oxygen inhalations to decompress a severely distended intestine. The establishment of this degree of pressure was purposefully effected in stages over a period of five hours, rather than abruptly, in order to simulate to some degree the clinical condition in which the tension accumulates over a period of hours or days rather than minutes.

Results—When the small intestine of the cat, ligated at the pylorus and ileocecal valve, is gradually distended with air to a pressure of 800 Mm of water in accordance with the technic described above, the subsequent course of events, in the average instance in an animal breathing air, is as follows. There is a slow and steady decline in the intraluminal pressure for a few hours to an average minimum of 433 Mm of water, with extremes varying from 130 to 774 Mm of water. The physiologic processes operating to reduce

*The intra-enteric pressure in mechanical obstruction of the small intestine in man has been observed to vary between 40 and 140 Mm of water pressure, with increases as high as 300 Mm during peristaltic activity.⁶ Such determinations of the intra-enteric pressure, unless made under constant volumetric conditions, may be considered lower than the actual values. We have observed in the cat a drop from 364 Mm of water pressure to 277 Mm upon the withdrawal of 25 per cent of the total gas volume in the bowel, and from 277 to 91 Mm when 7 per cent was withdrawn. Hence a leak around the needle injected into the bowel, or an appreciable displacement of gas into the manometric system, will register a pressure below its true value.

the initial pressure may be threefold (1) The nitrogen diffuses slowly into the blood stream (and possibly into the peritoneal cavity) because its tension in the intestine exceeds that in the blood stream and the surrounding tissues (2) The oxygen fraction of the injected air is absorbed rather rapidly. The rate at which this occurs in these distended animals, however, is slower than is to be expected normally, in proportion to the extent to which the blood supply in the intestinal wall is reduced by the increased intraluminal tension (3) Relaxation of muscle tonus or paralytic dilatation from prolonged overstretching of the bowel wall may reduce the tension

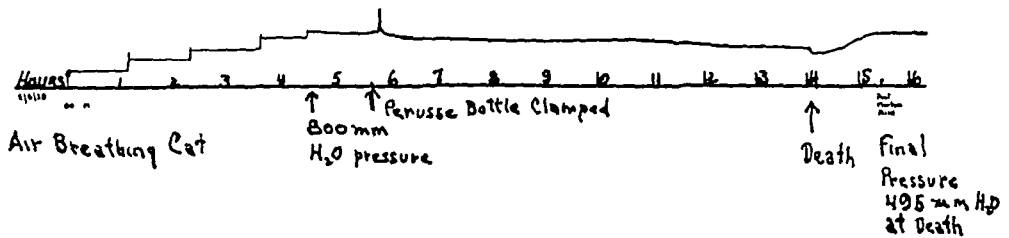


CHART 1—Kymographic tracing of intra enteric pressure of small intestine ligated at pylorus and ileocecal valve and inflated through a Perusse bottle with air in increasing increments each hour for five hours up to a maximum of 800 Mm of water. At the end of the sixth hour the Perusse bottle was clamped off and the animal was allowed to deflate spontaneously. Breathing room air. Death occurred eight hours later with final pressure of 495 Mm of water.

Once the minimum pressure is attained it usually remains unchanged until death of the animal occurs (Chart 1). In four of the 12 cats breathing air, however, a subsequent rise in pressure occurred (Chart 2), which in three cases exceeded the initial level of 800 Mm of water. The average survival time in those cats not showing this secondary rise was 11.7 hours. The average survival time in those which did show such a secondary rise was only 5.25 hours. In one such animal, the pressure fell from 800 to 700 Mm of water during the first hour, but in the following one and one-half hours it rose to 1,065 Mm of water and the cat expired, a survival time of only two and one-half hours. Another showed no drop from the initial level, the pressure rising steadily from 800 to 1,690 Mm of water in four hours, at which time death occurred.

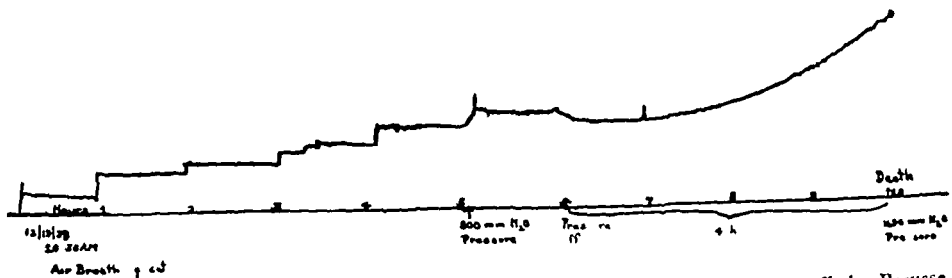


CHART 2—Same as Chart 1. Secondary rise in pressure one hour after clamping off the Perusse bottle and death four hours after Breathing room air.

We have no data to explain the mechanism underlying this secondary rise in pressure. Increase in muscle tone or the formation of gases in the bowel by bacterial action may account for it. It is clear from our autopsy data that it cannot be accounted for on the basis of increased fluid in the bowel lumen (Table I). Whatever the mechanism, it is important to note that when such

a secondary rise is superimposed on a long sustained high intra-intestinal pressure, death rapidly results. If such a phenomenon exists in man, its clinical importance in hastening death from overdistention is sufficiently clear and justifies unremitting effort to reduce a gaseous distention of a severe grade.

TABLE I

DISTENDED ANIMALS BREATHING ROOM AIR

Small intestine ligated at pylorus and ileocecal valve Cannula inserted into terminal ileum
Bowel inflated with air over period of six hours, in increasing increments, to a level of 800 Mm
of water pressure by means of Perusse bottle (in all cases except Exper. 8 in which nitrogen
was injected by means of a syringe to 1,015 Mm of water)

Experiment Number	Total Survival Time in Hours	Minimum Pressure in Millimeters of Water	Pressure at Time of Death in Millimeters of Water	Peritoneal Fluid in Cubic Centimeters	Fluid Content of Bowel in Cubic Centimeters	Ratio of Bowel Weight to Body Weight in Per Cent
1	29*	130	169	17	10	2 29
2	17	260	260	33	35	2 91
3	20	325	455	21	10	2 99
4	19	390	400	33	45	2 46
5	12½*	390	390	25	2	3 12
6	13	440	440	46		2 79
7	14	494	494	43	10	1 59
8	11	728	728	59	2	2 84
9	11	494	650	59	22	2 44
10	16	364	950	27	10	2 42
11	8½	700	1,065	21	2	2 68
12	10	774	1,690	36	15	2 16

* Sacrificed at time indicated

That reduction of the distention will prolong the life of the animal is to be expected. We wish now to present evidence that the inhalation of 95 per cent oxygen accomplishes this result by effecting a steady decline in the pressure level of the intestine distended by atmospheric air or nitrogen (Table II). Fourteen animals, prepared in exactly the same fashion as the

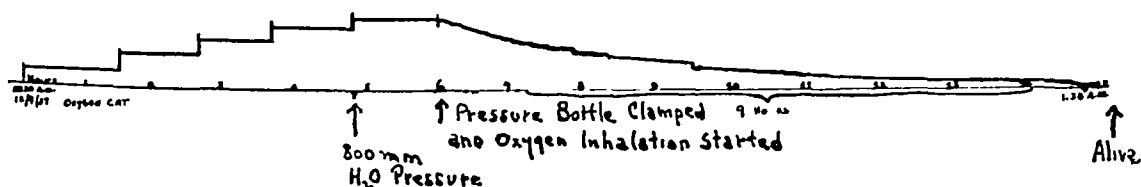


CHART 3—Same as Chart 1, except that the cat breathed oxygen instead of air from the time the Perusse bottle was clamped off until the end of the experiment. Animal alive, deflated and in good condition nine and one half hours later.

distended control group, were caused to breathe pure oxygen following the gradual establishment of an intraluminal pressure of 800 Mm of water by distention with atmospheric air or nitrogen. The course of events described above as occurring in cats breathing air is in definite contrast to that occurring

TABLE II

DISTENDED ANIMALS BREATHING PURE OXYGEN

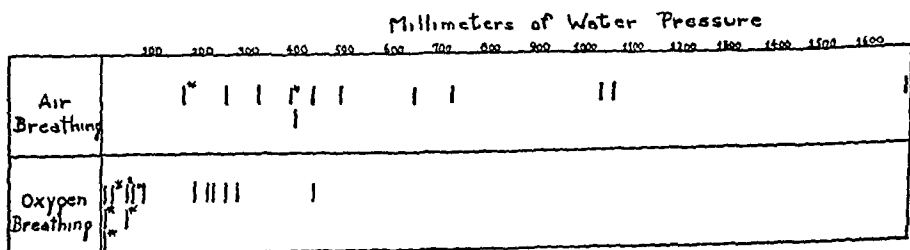
Small intestine ligated at pylorus and ileocecal valve Cannula inserted into terminal ileum Bowel inflated with air over period of six hours, in increasing increments, to a level of 800 Mm of water pressure by means of Perusse bottle (in all cases except Experiments 3, 11 and 13 in which nitrogen was injected by means of a syringe to 600, 1,430 and 1,220 Mm of water pressure, respectively)

Experiment Number	Total Survival Time in Hours	Pressure at Time of Death in Millimeters of Water	Peritoneal Fluid in Cubic Centimeters	Fluid Content of Bowel in Cubic Centimeters	Ratio of Bowel Weight to Body Weight in Per Cent
1	32*	0	24	5	3.37
2	19	0	25	0	3.01
3	18*	0	20	—	2.86
4	22*	19	8	21	1.7
5	26*	52			
6	29*	52	31	5	2.07
7	24*	65	33	0	2.49
8	27	78	23	15	1.78
9	17	195	28	10	2.14
10	19	225	29	10	2.77
11	18	234	38	10	1.59
12	14	260	19	23	2.56
13	17	286	30	15	2.62
14	17	442	46	10	3.11

* Sacrificed at time indicated

in those breathing oxygen. In the former, the intraluminal pressure, after an initial decline, leveled off to an average minimum of 433 Mm of water, while in the latter the pressure continued to fall until it reached a normal or nearly normal level (20 to 40 Mm of water⁵) in eight of the 14 animals (Charts 3 and 4). The average intra-enteric pressure reached was 136 Mm of water with extremes varying from zero in three instances to one with an

CHART 4



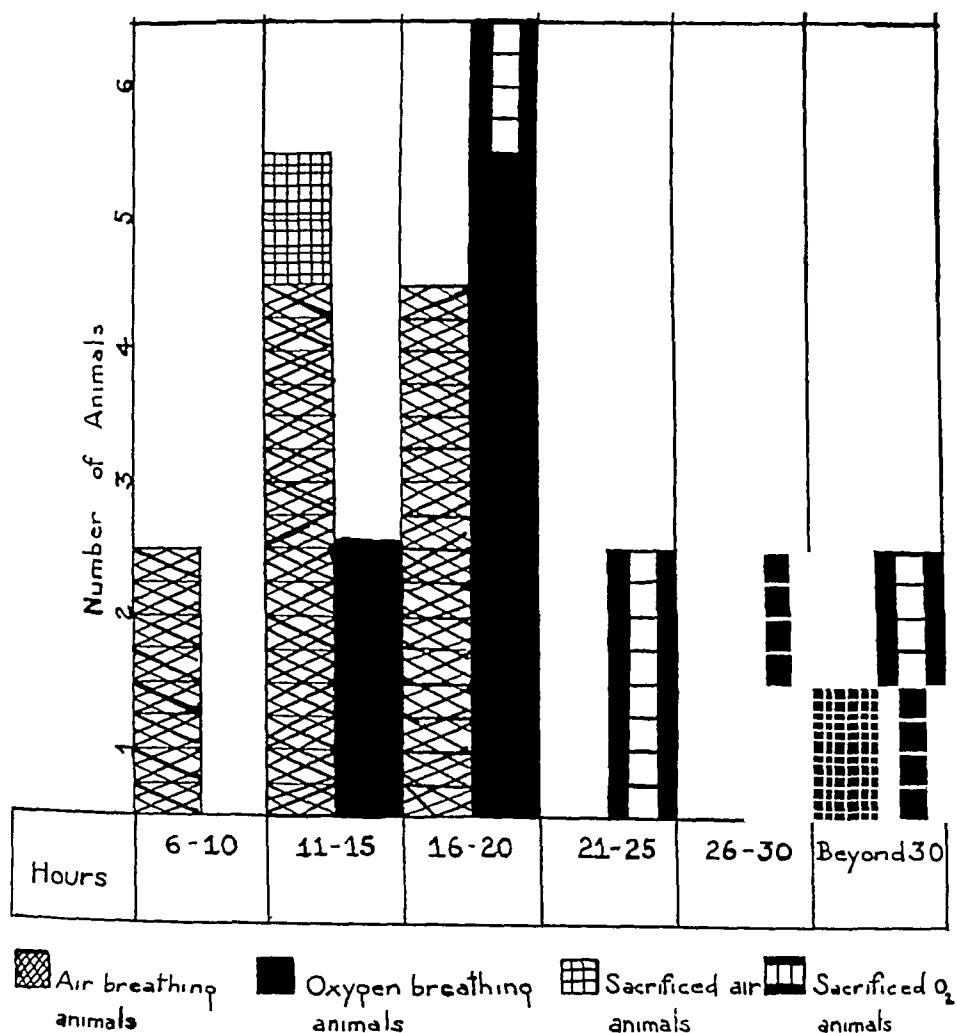
* Sacrificed

INTRAENTERIC PRESSURE AT TIME OF DEATH

exceptionally high level of 442 Mm of water. The secondary rise in pressure observed in four of the air breathing animals did not occur in any of those breathing oxygen.

Concomitant with the greater reduction in intra-enteric pressure there was a notable prolongation of the survival time (Chart 5). Six animals died with an average survival time of 188 hours following the establishment of the initial pressure level of 800 Mm of water, as against an average survival time of 85 hours for those animals breathing air. Six others breathing oxygen were sacrificed while still in good condition after an average survival of 25 hours. Two cats which were distended with nitrogen up to an initial level of 1,220 and 1,430 Mm of water pressure lived 17 and 18 hours respectively.

CHART 5



SURVIVAL TIME

The initial drop in pressure during the first one to three hours was of much the same order of magnitude in both oxygen and air breathing animals (compare Charts 1 and 3), although two of the latter did not show even this preliminary drop. One might expect the oxygen breathing animals to show a more precipitous fall in pressure during this early period than those breathing air. Its failure to occur is explained by the fact that a latent interval of three to four hours, during which the blood stream becomes desaturated of the nitrogen dissolved in it, is necessary before nitrogen in any quantity begins

to diffuse from the bowel lumen into the blood stream with resulting decompression⁹

The peritoneal fluid recovered at autopsy from the animals breathing air averaged 33.3 cc, while that recovered from those breathing oxygen averaged 27.2 cc. In a corresponding group of four animals, similarly treated but not distended, the peritoneal fluid averaged 6.5 cc, which was chiefly blood incidental to operative manipulation. The distended animals, therefore, showed an average excess of 24 cc of peritoneal fluid, which is directly attributable to the prolonged distention of the intestine. Since this fluid loss is of equal magnitude in the oxygen and air breathing animals, it cannot be regarded as a factor in the more rapid death of the latter. The volume of fluid in both groups, even if regarded as a loss of circulating blood, represents only about 11 per cent of the total blood volume and is consequently not an adequate cause for the death of the animals in either group.

If the peritoneal fluid is to be explained as a transudate from engorged capillaries resulting from partial or complete venous occlusion, one might expect for the same reason a simultaneous increase in the fluid content of the intestine above that which is found in a nondistended gut. An increase in intraluminal fluid was, however, not observed. The average fluid content of the distended intestines in the oxygen and air breathing groups was about 13 cc as compared to 11 cc in the series of four similarly prepared but undistended animals. If excessive intra-enteric transudate does occur at some stage in the period of distention, one should expect to find in it those animals whose pressure remained high (well above normal venous pressure) up to the time of death. The data in Table I show no parallelism between final pressure and fluid content of the bowel. This is in accord with the findings of Gatch,⁶ *et al*. There is an apparent contradiction between this finding and the well known clinical fact that overdistended and obstructed intestines usually contain excessive quantities of fluid. The animals studied in these experiments were starved and their intestines were relatively empty. In man the excessive fluids are probably to a large extent due to more or less fluid and

TABLE III

UNDISTENDED CONTROL ANIMALS

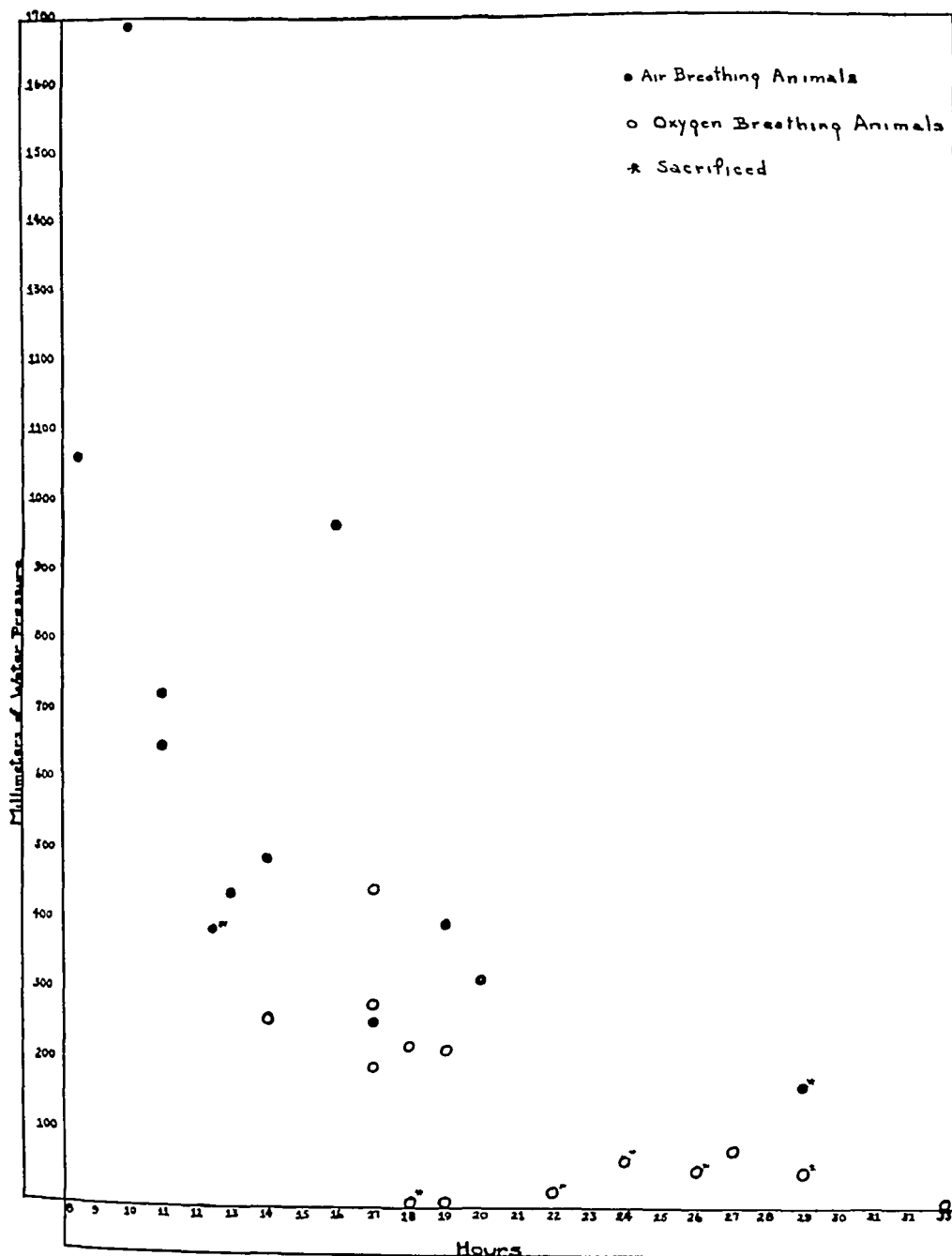
Small intestine ligated at pylorus and ileocecal valve Cannula inserted into terminal ileum

Experiment Number	Survival Time in Hours*	Peritoneal Fluid in Cubic Centimeters	Fluid Content of Bowel in Cubic Centimeters	Ratio of Bowel Weight to Body Weight in Per Cent
1	35	2	5	1.66
2	21	11	20	2.79
3	17	11	8	2.56
4	37	2	10	3.06

* Death in these animals due in part to regurgitation of citrate into the blood stream during continuous blood pressure observations

food intake immediately preceding the onset or during the period of distention. There is no evidence in these experiments to substantiate Van Zwahlen-burg's⁷ observation that the bowel mucosa at a distention pressure of 60 Mm

CHART 6



RELATIONSHIP BETWEEN SURVIVAL TIME
AND INTESTINAL PRESSURE AT TIME OF
DEATH

Hg "sweats" sufficiently to account for the increased fluid in the obstructed intestine in man. This does not, however, negate the possibility that excessive quantities of intraluminal fluid may accumulate at the pressure levels ordinarily observed in distention in man, which are very much lower than we have uti-

lized in these experiments and which have usually been established for a much greater period of time

An average of the ratios of the weight of the small intestine to the weight of the animal shows no significant difference between distended and undistended animals (Tables I and III). There is, therefore, no evidence of an important loss of blood volume into the wall of the distended intestine. This agrees with similar findings by And⁸ for closed loop obstruction. The evidence, therefore, is against fluid loss into the peritoneal cavity, bowel wall and bowel lumen as an explanation of the more rapid death of animals with high degrees of gaseous distention.

Of interest is the relationship between the survival time of the entire 26 distended animals and their intraluminal pressure at the time of death. Chart 6 shows that those animals with the lowest intraluminal tension appreciably outlived those which were unable to adequately decompress themselves, while high terminal pressures, as occurred in four of the distended animals breathing air, resulted in very early death.

Comment—The pathologic changes in ileus, aside from those due to actual strangulation, are produced by intra-enteric pressure alterations resulting from the accumulation of gas and fluid within the bowel lumen. The central problem in the therapy of obstruction, whether mechanical or functional, is the relief of increased intra-intestinal pressure. When the indications for surgical relief are clear, there is no better solution of the problem. Lacking such indications, the ordinary procedures for deflation are utilized, but unfortunately fail all too often. In such cases breathing 95 per cent oxygen, in accordance with a technic already described,³ provides a method for effective deflation. Our experimental studies prove that breathing pure (or 95 per cent) oxygen results not only in a striking decrease in gas volume¹ but also in a marked reduction in the pressure within the lumen of the intestine. The lethal effects of a sustained high grade gaseous distention are thereby delayed or entirely avoided.

SUMMARY AND CONCLUSIONS

(1) When the obstructed small intestines of a group of 12 cats were distended with air or nitrogen up to a level of 800 Mm. of water pressure, death ensued in eight of these animals within an average of 11.7 hours following the establishment of this pressure level.

The intra-intestinal pressure in these eight animals fell from the initial level of 800 Mm. of water to an average minimum of 433 Mm. of water.

In the remaining four animals of this group a secondary rise in pressure occurred with resulting rapid death after an average survival time of only 5.25 hours.

(2) In a group of 14 cats, similarly treated, but breathing pure oxygen from the time the initial pressure level was established until termination of the experiment, the survival time was much longer. The average was 18.8 hours for eight animals which died and 25 hours for six which were sacrificed while still in good condition.

Eight of this group reached a final intraluminal pressure within or close to normal limits (20 to 40 Mm of water), while the remaining six reached an average final pressure of 273 Mm of water pressure

(3) Evidence is offered to show that gaseous distention produces an increase in peritoneal fluid, but no appreciable change in the weight of the bowel wall. When the entire small intestine of the starved cat is converted into a closed loop distended with air to a pressure of 800 Mm H₂O, there is no increase in the fluid content of the intestine

The shorter survival time of the air breathing distended animals cannot be accounted for on the basis of fluid loss into the peritoneal cavity, bowel wall and intestinal lumen

(4) Breathing pure oxygen is an effective means of reducing the intra-intestinal pressure and of prolonging the survival time of cats in which the obstructed small intestine is distended with air or nitrogen

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IMPORTANT STEPS IN ASEPTIC INTESTINAL ANASTOMOSIS

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CERTAIN axioms have been accepted in regard to this problem. It is agreed that such a resection may not be strictly aseptic. It is well known that a Lembert type of suture occasionally enters the intestinal lumen and is thus contaminated. However, the degree of asepsis maintained can be made greatly superior to that obtained in an open operation. The results following such an aseptic technic indicate that if there has been some degree of contamination, it has usually been cured for without reaction.

In 1922, the writer¹ detailed a procedure which had been developed to effect an aseptic intestinal resection, and has keenly watched the interest that has been manifested in the subject since that time. As steps in the technic have been developed, surgeons now are generally accepting the aseptic technic of resection, where indicated, as superior to open methods. In an attempt, possibly, to standardize an aseptic technic, the writer wishes to emphasize steps that seem, to him, essential. Conditions requiring resection are often found unexpectedly, and in order that an aseptic method can be employed, when indicated, the method should be uncomplicated and adaptable to the instruments usually found in any surgical armamentarium.

In many of the contributions on this subject, we feel that three features have been overemphasized. First, that the inturned intestinal cuff is objectionable, second, that the first row of sutures should be interrupted mattress sutures, and third, that the crushing forceps should be quite narrow. In regard to the first point, Halsted,² his coworkers, and others, have shown that the inturned cuff soon disappears—the crushed portion by sloughing and the remaining by atrophy. In 62 resections that we have performed, by the method to be described, there has not been a symptom to indicate an obstruction, or other undesirable features, produced by the cuff. It is of more importance to have the suture line coapt the intestinal surfaces without tension, than to be greatly concerned about a slightly larger inturned cuff. As for the second point, namely, concerning interrupted mattress sutures in the first row, such sutures have many knots to bury and invite subsequent trouble. They strangulate the area they include, producing pressure necrosis, and afford a greater danger of leakage at such a point. Again, with interrupted mattress, or for that matter any type of interrupted suture in the first row, with the onset of distention of the intestine, the sutures become further separated and intestinal contents may escape. With a well placed

continuous suture, the intestinal distention tends to tighten the suture line. As for the third point—in regard to the size of the crushing forceps—it has been our experience, since the intestines are not handled but are held in position entirely by these forceps while the first suture row is being placed, that the forceps should be fairly wide and strong enough to crush and hold firmly. A narrow forceps will occasionally cut through or slip off at a crucial moment. A wider crushed portion of cuff will always slough away. The forceps should not have toothed tips, but should be rather of the ordinary straight Pean type, so that they will pull out easily after the first row of sutures is completed. The accompanying plate of illustrations will perhaps serve to emphasize the steps of the operative procedure we have employed.

Figure 1 (A)—The blood supply, especially in the colon, must be without question. An opening is made in the intestinal border of the mesentery near a well defined arterial branch. The intestinal wall is stripped clean of mesentery toward the segment to be resected, so that twice the width of the crushing forceps is cleared between the artery and the tip of the forceps. All surfaces of the intestine to be approximated by sutures must also be freed from fat tags or other extraneous tissues, so that peritoneal surfaces may come in contact. If after resection the blood supply to the parts to be anastomosed seems impaired, reapply other forceps in the same manner and again resect, until a good blood supply is demonstrable. Avoid handling the unresected portion of the intestine. Do not strip away its contents or apply any ligatures or rubber-covered forceps to hold the contents away from the crushing forceps.

(A) The exact manner of applying the crushing forceps in an end-to-end anastomosis is most important. The tip of the forceps must be placed exactly at the mesenteric border of the intestine in the cleared space—the proper distance from the arterial branch. If the tips extend beyond the border, they cannot be properly buried by the first suture row, and thus assure against leakage at that point when the forceps are withdrawn upon completion of that row. The crushing forceps can be applied at right-angles to the intestine, or, to make a larger lumen or to improve the blood supply, at an angle away from the part to be resected. If the lumina of the two ends to be anastomosed are not of the same size, the smaller end can be enlarged by resecting it at an angle, or a removable loop-ligature¹ can be applied to the larger end and the forceps applied over this to contract that end down to approximate that of the smaller one. A second straight forceps of any type is applied alongside the first and the intestine is cut through with a thin bladed cautery.

(B) After resecting and observing that the blood supply of both ends to be anastomosed is sufficient, the operator holds both Pean forceps in one hand with the cauterized ends of the intestine in apposition, the tips of the forceps even without rotation. He thus holds them throughout the placing of the first row of sutures. Crushed ends of intestine, with forceps removed before tying of sutures, cannot be depended upon to hold. Forceps left in

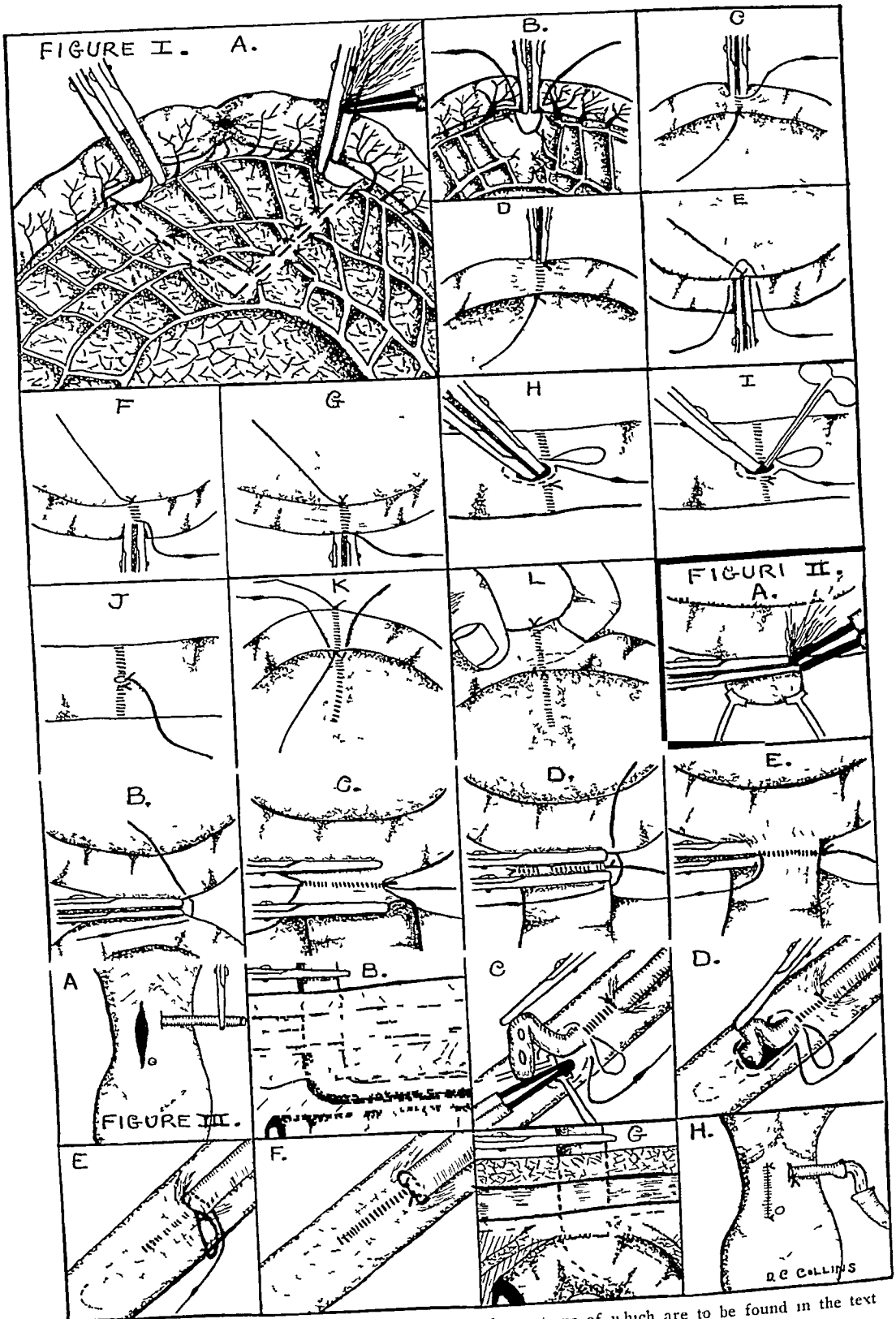


PLATE I—Incorporating Figures I, II and III, descriptions of which are to be found in the text

place while suturing are secure, assure a minimum handling of the intestine and are most convenient for holding a constant position

Suture material for the first row, we believe, should be absorbable, chromic intestinal catgut mounted on a straight atraumatic intestinal needle, thus enabling the operator to estimate more accurately what intestinal layer is being transected. Nonabsorbable suture material is cast off into the intestinal lumen. But when it is only partially extruded into the lumen, it may adhere to the intestinal canal, catching material and thus producing a possible degree of obstruction

(B) The first stitch is of especial importance and is that one which is placed in the cleared space at the mesenteric border, between the arterial branch and the tips of the forceps on either end. It is so placed that when tied, the intestinal walls are drawn over the ends of the forceps so as to bury the tips. The suture end is left long so that it may be tied to a second suture, to be later placed in the opposite side

(C) The tips of the forceps are now depressed and the suture continues as a continuous running Lembert suture covering in the forceps, as seen from the operator's side, and is tied when the shanks of the forceps are reached (D)

(E) The operator now, without changing the approximation of the forceps, rotates them in order to bring the other side of the intestine into view. A new suture is then started at the tips of the forceps, as in the first suture (F), and when it is tied, and retied to the end of the first suture already in place, the tips of the forceps are securely buried and there can be no gap at the mesenteric border in the first suture row. (G) This second suture is continued, as on the opposite side, until the shanks of the forceps are reached. (H) It is then purse-stringed around the shanks of the forceps and (I and J) is drawn snugly and tied as the forceps are removed. A suggestion is essential relative to the removal of the forceps: they are loosened and removed, one at a time, as the purse-string suture is tightened. There is a tendency for the crushed ends of the intestine to adhere to the forceps as they are withdrawn. (I) A small forceps or probe held on the cuff at the border adjacent to the crushing forceps, as it is withdrawn, will keep the cuff within the intestinal lumen.

(K) By holding the ends of the first row of sutures, the suture line is kept on tension and the second row is applied, not too closely, nor so tightly as to cause pressure necrosis. Started at the mesenteric border, this suture should close the split of the mesentery as it divides to go around the intestine, but care must be taken not to involve the arterial branch thus far preserved. This second row can be either of absorbable or nonabsorbable material, continuous or interrupted sutures. In the colon, a second row of absorbable material and a third row of nonabsorbable interrupted sutures may be advisable. (K) The closure of the mesenteric gap is made in the usual manner observing care again not to involve the important blood supply to the intestinal wall. (L) At this stage do not neglect to pass the tips of the thumb and a finger through the anastomosis to free the agglutinated ends of the

cuffs One is surprised to find the ample lumen that is thus demonstrated An omental tag or a free omental graft covering the suture line is an additional safeguard against leakage, particularly in a colon resection

Figure II (A)—In a side-to-side anastomosis an ample pouch of intestinal wall is pulled up and clamped across, the tip of the Pean forceps not extending beyond the intestinal surface This protruding portion of wall is excised between forceps with the cautery and the suturing is done (B) in an analogous manner as described for an end-to-end anastomosis (C and E) However, as in performing an end-to-side ileocecostomy, or an ileotransverse colostomy, it may be best to place the two posterior rows first so as to facilitate suturing

Figure III—A number of times after resecting, we have thought it advisable, because of some degree of suspected ileus, to place an enterostomy tube proximal to the resection in order to prevent dangerous distention Our concept concerning enterostomy is that the tube should be inserted for decompression in anticipation of trouble, rather than after symptoms are well established In high resections of the small intestine, the use of the nasal duodenal tube for decompression, as suggested by Wangenstein,³ may be employed in place of enterostomy, provided the tube is not allowed to reach the site of anastomosis In resection of the left or transverse colon, a cecostomy performed as a first-stage operation decompresses both before and after resection If an enterostomy tube is inserted, it should also be accomplished by an aseptic technic (A) Through a stab wound of the abdominal wall, at one side of the incision, a fairly stiff No 12 or 14 F rubber catheter, with a clamp on its outer end (B), is passed into the abdomen and through the omentum About 20 cm proximal to the anastomosis, the tube is laid along the antimesenteric axis of the intestine that has been stripped of its contents and clamped off with soft rubber-covered forceps (C) With a chromic intestinal suture on a straight atraumatic intestinal needle, a continuous Lembert suture buries the tube snugly for about 5 cm Approximately 7 cm of the tip of the catheter is left uncovered, turned up, and the same suture is purse-stringed about an area through which a puncture is to be made by cautery into the intestinal lumen The cautery is employed after Allis forceps are applied within the purse-string suture to hold up the intestinal wall, and thus guards both the purse-string and the opposite intestinal wall from damage

(D) The tip of the tube is guided into the cautery puncture with a forceps (E) The purse-string is pulled tight, and the same suture continued back as a second invaginating row to the starting point (F) At this point the suture is tied so as not to cut too tightly into the wall of the intestine Against this knot the same suture is tied tightly about the catheter to anchor it in place (G) The tube is then drawn up through the abdominal stab incision, drawing the enterostomy site snugly against the peritoneum with the omentum intervening (H) A suture of nonabsorbable material is passed through the skin edge of the stab wound, tied loosely, and against

this knot, the tube is secured, giving it a second anchorage at this point

The enterostomy tube is connected up for drainage and is kept open by injecting small quantities of warm, normal saline solution frequently, if indicated. The escape of gas alone may be all that is required to prevent distention. After a few days, when indicated, the skin suture is cut and the catheter is allowed to come away of its own accord. In the cases that we have operated upon in this manner, there were no fistulae that did not close spontaneously.

We have now resected, by the method described above, 19 of the colon and 43 of the small intestine, a total of 62 cases. In a *first group* of 36 cases, the condition of the intestinal wall seemed sufficiently good to allow of resection. These conditions were: Ten early strangulations, four of massive adhesions, three Meckel's diverticula, one stricture of the colon, one gastriocolic fistula, one granuloma of the terminal ileum, eight carcinomata of the colon, three duodenojejunosomies for duodenal obstruction, four ileo-transverse colostomies for carcinoma of the ascending colon, and one colo-colostomy for benign stricture of the sigmoid colon. In this group of cases, one died (2.8 per cent), a gastriocolic fistula, a portion of the stomach, jejunum, and colon being resected. A leakage occurred in the suture line of the transverse colon, resulting in a subsequent fatal peritonitis. This patient was a very poor risk from general inanition.

In a *second group* of nine resections the general conditions were poor, consisting of late obstructions with toxemia, and having intestinal walls that were questionable for suturing. In two cases pneumonia developed, which proved fatal. This group included one granuloma of the terminal ileum and cecum, five gangrenous, obstructed small intestines, one volvulus of the colon, and one carcinoma of the descending colon. In this group there were four deaths (44.4 per cent), one volvulus of the colon, one carcinoma of the splenic flexure of the colon, and two very extensive resections for gangrenous strangulated ileum.

A *third group* of 17 resections were performed in 16 late obstructions of the ileum in whom ileus and toxemia were well established, when no type of operation offered other than a forlorn hope. Of these, 16 died (94.1 per cent). One case of carcinoma of the splenic flexure of the colon survived.

CONCLUSIONS

Of a total of 19 colon resections in the three groups, 16 (84.2 per cent) recovered. Of the three that died, two cases did not have a preliminary decompression because conditions did not permit.

If the 16 deaths in the third, apparently hopeless group can be eliminated from this consideration, there were then 46 resections in groups one and two with five deaths, a mortality of 10.8 per cent.

We believe that enterostomy, performed at the time of resection, is indicated in some cases to help recovery of the intestine by preventing distention and ileus. This is particularly true in such cases as are represented by

groups one and two We have proved its value in a large group of cases, not included in this paper, where strangulating bands were freed without resection However, enterostomy seemed without value in such cases as represented by group three

If the condition of the intestinal walls justifies suturing, aseptic resection can be undertaken with confidence

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TRANSIENT ACUTE PANCREATITIS*

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THERE has been a notable trend in recent years to distinguish between two groups of acute pancreatic disease. The picture of acute pancreatitis characterized by a fulminating attack of epigastric pain associated with massive necrosis of the pancreas and fat necrosis of the peritoneal structures is well known. Included in this group and probably representing different stages of the same pathologic process are the so-called "acute hemorrhagic pancreatitis," "acute suppurative pancreatitis" and "acute pancreatic necrosis." The other group, which has only recently obtained more concise definition, has been variously termed "acute pancreatic edema" by Zoepffel¹ and Archibald,² "subacute pancreatitis" by Stetten,³ "acute interstitial pancreatitis" and "acute transient disease of the pancreas" by Elman.^{4, 5} It is with this latter group that our study is primarily concerned.

Penín⁶ attributed the earliest descriptions of edematous pancreatic lesions to Salsted (1890), Villard and Brance (1909), and Mercade (1919).

Zoepffel (1922) described a group of four operated cases of acute pancreatitis characterized by a complete lack of necrosis, and a glossy edematous infiltration of the pancreas, lesser omentum and transverse mesocolon. Microscopic examination of sections excised from two cases showed a marked interstitial and interlobular edema.

Archibald (1929) described experiments in cats in which he caused bile to flow through a small cannula from the common bile duct into the main pancreatic duct. Within a few minutes there developed a marked edema of the pancreas which subsided the following day. He described one case of presumptive, acute edema of the pancreas in a young man. Such a condition, he felt, occurred with unrecognized frequency, and probably explained some cases of acute epigastric pain diagnosed inaccurately as biliary colic, acute intestinal obstruction, perforated peptic ulcer, *etc*.

Elman (1933) made a thorough review of the literature and collected 37 cases of "acute interstitial pancreatitis" including four of his own, in all of which edema and induration of the pancreas were demonstrated. In 1935, he⁷ added six more cases to this series. Again in March, 1937, he⁵ presented eight cases of presumptive, acute pancreatic disease of a transient nature, four with operative findings. Since the review by Elman,⁴ in 1933, this type of lesion has been mentioned by Bachy,⁸ Dragstedt, Haymond and Ellis,⁹ Penín,⁶ Vianna,¹⁰ Mouroud and Doi,¹¹ May,¹² and Mahner.¹³

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The lesion generally associated with these cases is one of noninflammatory interstitial (interlobular and interacinar) edema, frequently with leukocytic infiltration^{1, 2, 3, 4, 6, 10} According to Archibald the lesion results from a reflux of bile into the pancreatic ducts, Elman thought it might be caused by a transient obstruction to the main pancreatic duct The relationship of acute pancreatic edema to pancreatic necrosis has been a subject of contention Zoepffel, Stetten, Bachy and Penín were of the opinion that edema of the pancreas was an early stage of acute necrosis Nordmann¹⁴ described several cases, observed both at early operation and at autopsy, which progressed from an edematous type of lesion to one of necrosis Schmieden and Sebening,¹⁵ Archibald, Leveuf,¹⁶ and May,¹² while agreeing that edema may be an early stage of necrosis, thought it frequently subsided without progression to fat necrosis Walzel,¹⁷ and Pólya (cited by Leveuf¹⁶) were not convinced of this relationship, but felt that acute edematous pancreatitis was a benign lesion which subsided spontaneously without progression to necrosis Because our cases lack surgical or postmortem confirmation we are not prepared to venture a definite opinion on the relationship of transient acute pancreatitis to acute pancreatic necrosis Using only clinical observations as the criteria upon which we based our conclusions, we are inclined to the opinion that progression to necrosis does occur, but the process can be interrupted spontaneously during any stage

We have confined our case reports only to those cases which we feel fall into the group of transient acute pancreatitis Cases of the necrotic, hemorrhagic or suppurative type, of which we have had several, have been excluded From the records of the Jewish and City Hospitals, St. Louis, during the past three years, we have collected 21 cases whose symptoms and laboratory findings bear sufficient resemblance to the cases of Zoepffel, Katsch,¹⁸ Archibald, Stetten, Elman, and others to warrant inclusion in this classification

CASE REPORTS

Case 1—E U, female, age 43, entered the City Hospital May 10, 1935, complaining of excruciating pain in the upper abdomen of one day's duration, accompanied by intense nausea and vomiting and followed by jaundice Temperature 98.8° F, pulse 112, leukocyte count 12,000

Examination disclosed a distinct icterus There was generalized abdominal tenderness, most marked in the epigastrium Muscle guard was limited to the epigastrium

Laboratory Data The blood diastase, determined on admission by Somogyi's method,² was 1,500, an extremely high level (see discussion on blood and urinary diastase, p 1037), but the following day it dropped to 168, a normal value, and there was an almost complete subsidence of pain Blood sugar 74 mg A plain roentgenogram of the abdomen revealed nothing significant Cholecystograms failed to visualize the gallbladder On May 21, 1935, the symptoms and abnormal physical findings having completely subsided, the abdomen was explored

Operation—A thin-walled gallbladder containing a few cholesterol stones was found The pancreas appeared normal both grossly and microscopically Cholecystectomy and appendectomy were performed The postoperative course was uneventful, and the patient was discharged June 2, 1935

This is a case of biliary tract disease complicated by a transient attack of acute pancreatitis. The fact that operation at a late date revealed no pancreatic pathology is of no significance since the pancreas usually reverts to a normal histologic appearance within several days after the attack.

Case 2—S. C., female, age 31, was operated upon in the Jewish Hospital April 25, 1935. In 1933, this patient had had an attack of sharp, sudden, severe upper right quadrant pain. These attacks had recurred several times during the next two years. On April 25, 1935, a cholecystectomy and choledochostomy were performed, and several small stones were recovered from the choledochus. At that time no diastase determinations were made.

Postoperative Course—Two weeks after the operation the blood diastase was 56, there had been no previous determinations made. The patient was readmitted June 21, 1935, complaining of severe, sharp epigastric pain which had begun the day before, associated with nausea and vomiting. During the night the pain had become less sharp in character, but continued as a constant soreness and radiated to the right costovertebral angle. Temperature 101.4° F, pulse 108, leukocyte count 12,600. There was marked epigastric and upper right quadrant tenderness but little rigidity. The liver was enlarged two fingerbreadths below the costal margin. There was a faint icteric tint to the skin. *Laboratory Data*—On June 22, 1935, the blood diastase was 708. By June 25, 1935, most of the symptoms had subsided, and the blood diastase had dropped to 100. The icteric index was 15. The patient was discharged June 29, 1937.

Whether the recent attack of pain was due to a transient pancreatitis or to a combination of a transient pancreatitis and an overlooked choledochus stone was not ascertained. The biliary tract must, however, be considered the etiologic factor of the pancreatitis. The importance of pancreatitis as a cause of recurrent pain following cholecystectomy has been previously pointed out by Elman.

Case 3—H. M., male, age 69, was admitted to the City Hospital December 2, 1935, complaining of epigastric pain of a week's duration. Two days before admission the patient had noticed the appearance of jaundice, and the following day the pain became more intense and sharper in character and vomiting began. There was intense itching of the skin. Temperature 100.2° F, pulse 76, leukocyte count 24,200.

Examination disclosed moderate tenderness and slight rigidity in the upper right quadrant and epigastrium. *Laboratory Data*—On January 4, 1935, the blood diastase was 660, blood sugar 99 mg, icteric index 90, and the pain had largely subsided. The following day the diastase had dropped to 150. Operation was refused and the patient was discharged December 8, 1935.

Case 4—W. T., male, age 60, was admitted to the City Hospital January 29, 1936, complaining of a sudden attack of severe epigastric pain, which had begun 12 hours previously. The patient had had "stomach trouble" for 11 years, consisting mostly of epigastric discomfort two to three hours after meals, there had not been any hematemesis or tarry stools. No diastase determination was made at the time of admission. A preoperative diagnosis of perforated peptic ulcer was made and an emergency operation performed. No ulcer was found. The liver was moderately swollen and biopsy revealed a mild acute hepatitis. No mention of the pancreas was made.

Postoperative Course—The patient was readmitted June 5, 1936, complaining of spasmodic, severe, sharp, cramp-like epigastric pains of several hours' duration accompanied by vomiting. Temperature 99° F, pulse 80, leukocyte count 30,000. *Examina-*

tion revealed marked tenderness and moderate rigidity in the epigastrium *Laboratory Data* The blood sugar was 70 mg The following day, after slight improvement had occurred, the diastase was 400 By June 8, 1936, the diastase had dropped to 66, and the blood sugar was 154 The patient was discharged June 11, 1936

This patient probably had two major attacks of acute pancreatitis While a major lesion of the bile ducts and gallbladder seems to have been ruled out, the microscopic appearance of the removed liver tissue, in conjunction with the high diastase and blood sugar values obtained after subsidence of the attack, suggest some degree of liver involvement (See the discussion on the relation of acute pancreatitis to biliary tract disease, p 1041)

Case 5—S H, male, age 50, was admitted to the Jewish Hospital February 17, 1936, five hours after the onset of generalized abdominal pain, most marked in the epigastrium, accompanied by severe vomiting An appendicectomy had been performed two years previously for an attack of lower right quadrant pain, otherwise there had been no previous abdominal complaints Temperature 98° F, pulse 96, leukocyte count 16,000

Examination disclosed moderate, upper right quadrant and epigastric tenderness and slight epigastric rigidity *Laboratory Data* The urine showed a three plus sugar and a trace of albumin The day after admission the blood diastase was 1,250 Simultaneous urinary diastase was 4,575 The blood sugar was 108 mg The following day there was a moderate improvement in symptoms, and the blood and urinary diastase determinations were respectively 136 and 1,150 A plain roentgenogram of the abdomen revealed nothing significant On February 21, 1936, after all symptoms had disappeared, the blood diastase was 100 The patient was discharged

Case 6—E M, female, age 56, was admitted to the City Hospital September 11, 1936, complaining of intermittent cramp-like epigastric pains of three days' duration accompanied by vomiting and slight jaundice For the past 25 years the patient had had less intense attacks of similar pain Temperature 99.6° F, pulse 90, leukocyte count 7,550

Examination elicited moderate epigastric and upper left quadrant tenderness and some rigidity *Laboratory Data* The following day, September 12, 1936, the blood diastase was 2,000, blood sugar 64 mg Two diastase determinations, on January 13, 1936, showed 600 The following day the patient left the hospital, preventing further studies Her symptoms had completely subsided

Case 7—L B, male, age 42, was admitted to the City Hospital September 18, 1936, with a history of intermittent, knife-like epigastric pain for five days, which, however, had become more intense during the past ten hours The patient had been a heavy drinker for several years, and was intoxicated when the present illness began Temperature 97° F, pulse 120, leukocyte count 13,000

Examination showed a middle aged male writhing with pain, and the skin was cold and clammy There was marked tenderness and moderate rigidity in the epigastrium *Laboratory Data* The blood diastase taken shortly after admission was 750 The following day the pain became more generalized and a slight jaundice appeared The blood diastase was 666, blood sugar 120 mg Two days later, after considerable symptomatic improvement, the diastase was 132, and the icteric index 100 On September 23, 1936, the diastase had remained the same, but the icteric index had fallen to 40 Cholecystograms, September 28, 1936, revealed a normal functioning gallbladder The patient was discharged October 3, 1936

The history of alcoholism complicates this case In addition to the presence

of an acute pancreatitis the patient probably also had a toxic hepatitis which may have accounted for the appearance of jaundice

Case 8—F S, female, age 68, was admitted to the City Hospital October 19, 1936, with a history of intermittent, generalized abdominal cramp-like pains of one day's duration, during the last few hours they had become more constant. Several similar, but much milder, attacks had occurred during the preceding few years. Temperature 102.4° F, pulse 130, leukocyte count 14,500.

Examination showed a markedly obese, elderly female, with labored respirations, resulting from the pain, and perspiring freely. A slight degree of icterus was noted. There was moderate epigastric and upper right quadrant tenderness and slight rigidity. A sensation of fulness in the left hypochondrium was noted. *Laboratory Data* On the day following admission the blood diastase was 600, blood sugar 103 mg, icteric index 50. On October 21, 1936, much symptomatic improvement occurred, and the blood diastase dropped to 180. Further work-up was refused and the patient was discharged.

Case 9—T C, female, age 51, was admitted to the Jewish Hospital February 18, 1936, 24 hours after the onset of sharp epigastric pain which radiated to the interscapular region, and was accompanied by vomiting and severe headache. For two years she had had recurrent attacks of epigastric and upper right quadrant pain of a less severe character, which were interpreted as originating from a pathologic gallbladder. This diagnosis was substantiated by a cholecystographic examination which revealed a poorly filling and moderately enlarged gallbladder. Temperature 98.6° F, pulse 86, leukocyte count 12,000. There was no icterus.

Examination elicited marked epigastric and moderate upper right quadrant tenderness and rigidity. The liver was enlarged two fingerbreadths below the costal margin. *Laboratory Data* On February 19, 1936, 12 hours after admission, the blood diastase was 1,155, blood sugar 86 mg. The following day there was a notable improvement in her symptoms and signs, and the blood diastase dropped to 250. The urinary diastase at that time was 1,250. Sugar tolerance test gave a normal curve. On February 24, 1936, the blood diastase was 167. Five days later she was discharged.

The patient was readmitted August 3, 1936, with a similar, but more colicky attack of epigastric pain of 12 hours' duration. Temperature 98.6° F, pulse 86, leukocyte count 13,400. Her physical findings were similar except that, in addition, left costo-vertebral tenderness was noted. *Laboratory Data* Blood diastase determined the day following admission was 1,500, and the urinary diastase 3,000. After symptomatic improvement, two days later, the blood diastase fell to 220. Cholecystograms, September 7, 1936, showed no gallbladder visualization.

Operation—September 11, 1936. A celiotomy was performed. The gallbladder was removed and was found to contain many small, faceted cholesterol stones. The dilated choledochus contained several similar stones, and was drained. The pancreas was moderately enlarged and indurated, but no biopsy was taken. The postoperative course was uneventful.

This case presented two major attacks of acute pancreatitis of unquestioned biliary tract origin. The absence of obstructive common duct signs at any time is of interest in view of the finding of choledochus stones.

Case 10—J R, male, age 47, in 1928 had a cholecystectomy performed, at the Jewish Hospital, for a pathologic, calculous gallbladder. Four years later he developed an attack of upper right quadrant pain, suspicious of biliary tract colic. The following year (1933), after having had several similar attacks, he was reoperated. The common bile duct was thoroughly explored but no stones were found. One section of the choledochus presented a suggestive constriction. Since then similar recurrent attacks

of pain accompanied by vomiting, but without jaundice, have occurred. His most recent attack began on November 18, 1936. Two days later, after most of his symptoms had subsided, the blood diastase was 213, blood sugar 98 mg. Two urinary diastase determinations were 5,333 and 4,570. The following day the blood diastase had dropped to 94 and the urinary diastase to 1,600 and 1,450. On November 27, 1936, the blood diastase was 107 and the urinary diastase 800 and 460.

It is probable that most, if not all, of this patient's recurrent attacks of epigastric pain following cholecystectomy were the result of transient attacks of acute pancreatitis. While the initial blood diastase determination was not unusually high, it having been taken during the recession of the attack, the urinary diastase, which lags in its changes behind the blood diastase, was still considerably elevated. This indicates that the blood diastase was higher in the earlier stages of the attack than at the time it was determined.

Case 11—I K, female, age 32, was admitted to the Jewish Hospital January 17, 1937, with a history of intermittent, moderately severe colicky pains in the epigastrium and upper right quadrant of four days' duration, radiating to the interscapular region. Vomiting and flatulence were prominent symptoms. During the previous five years there had been several similar but less severe attacks. Temperature 101° F, pulse 90, leukocyte count 12,900. The skin was slightly icteric.

Examination elicited moderate epigastric and upper right quadrant tenderness and rigidity. The following day most of the symptoms and signs had subsided. *Laboratory Data* The blood and urinary diastase determinations were respectively 400 and 6,400, blood sugar 112 mg. The following morning the blood diastase had dropped to 110. Cholecystograms showed no gallbladder shadow. A plain roentgenogram revealed suggestive evidences of calculi. The patient was discharged January 22, 1937.

Case 12—B G, male, age 67, was admitted to the City Hospital March 23, 1937, with a history of sudden, severe, sharp epigastric pain of four days' duration followed by jaundice. Since the onset, the pain had become less severe but intermittent recurrences of a colicky nature occurred. Several years previously the patient had had a similar attack. Temperature 100.2° F, pulse 100, leukocyte count 18,200. A distinct icteric tint to the skin was noted.

Examination elicited moderate epigastric and upper right quadrant tenderness but no rigidity. The patient was apparently improving at the time he was admitted. *Laboratory Data* Blood diastase values, determined in the morning and afternoon, were respectively 600 and 392, blood sugar 123 mg, there was no glycosuria. The following day the diastase fell to 240, but the blood sugar rose to 176 and the urine showed a four plus sugar reaction. The patient was discharged March 21, 1937, no further work-up having been permitted.

The appearance of hyperglycemia and glycosuria during the fall in blood diastase is not an uncommon occurrence. It can be explained on the assumption that a certain amount of liver damage has occurred. (See discussion under carbohydrate tolerance, p 1041.)

Case 13—I T, female, age 39, was admitted to the City Hospital April 17, 1937, complaining of intermittent, severe colicky pains in the epigastrium and right upper quadrant of eight days' duration radiating to the right scapula. Nausea was severe, but vomiting had occurred only once on the day before admission. A number of similar but less severe attacks had occurred during the previous 15 years. Temperature 99.4° F, pulse 76, leukocyte count 12,300.

Examination showed the edge of the liver three fingerbreadths below the costal

margin, it was quite tender. Moderate tenderness and slight rigidity in the epigastrium were present. By April 19, 1937, some improvement had occurred. *Laboratory Data* April 19, 1937. The blood diastase values morning and afternoon were respectively 1,396 and 780, blood sugar 78 mg, icteric index 3. By March 24, 1937, blood diastase had fallen to 60. Three days later cholecystograms revealed a normal functioning gallbladder, and the patient was discharged.

Case 14—E. H., female, age 60, was admitted to the City Hospital April 30, 1937, complaining of an attack of excruciating upper abdominal pain of six hours' duration radiating to both scapular regions and accompanied by vomiting. Temperature 97.8° F, pulse 98, leukocyte count 8,640. The respirations were labored.

Examination elicited marked tenderness of the entire upper abdomen, but no rigidity. *Laboratory Data* May 1, 1937. The morning and afternoon blood diastases were respectively 1,998 and 1,710, blood sugar 122 mg. The following day there was considerable symptomatic improvement and the diastase was 1,092. By May 3, 1937, the patient was greatly improved, the blood diastase had fallen to 168, and she was discharged.

Case 15—F. K., female, age 45, was admitted to the Jewish Hospital February 11, 1935, complaining of sudden, severe epigastric cramping pain of ten hours' duration accompanied by vomiting. Temperature 99.6° F, pulse 95, leukocyte count 20,250.

Examination elicited a moderate amount of tenderness confined entirely to the epigastrium, but no rigidity. The following day there was some symptomatic improvement, but a moderate tenderness persisted. *Laboratory Data*. The blood diastase at that time was 570 and the blood sugar 196 mg. No glycosuria was noted. On February 14, 1935, a sugar tolerance test showed a markedly diabetic curve, and the patient was placed on a diabetic regimen. At that time, except for slight residual epigastric tenderness, the symptoms and signs had subsided. On February 16, 1935, the blood diastase was 180, blood sugar 74. Cholecystograms, February 27, 1935, revealed a normal functioning gallbladder. A second sugar tolerance test, February 28, 1935, showed a better carbohydrate tolerance. The patient was discharged March 7, 1935. A subsequent sugar tolerance test showed a normal curve.

This case offers an excellent example of the decreased carbohydrate tolerance sometimes associated with an attack of acute pancreatitis. (See discussion under carbohydrate tolerance, p. 1041.) While this patient was at first considered diabetic, subsequent analyses did not bear out this conclusion.

Case 16—S. C., female, age 68, was admitted to the Jewish Hospital April 26, 1937, for study following a series of attacks of upper right quadrant pain radiating to the right shoulder and back. These attacks began several months after a cholecystostomy had been performed, five years before, for acute gangrenous cholecystitis. She was a known diabetic, and had been well controlled under a dietary regimen.

Subsequent Course and Laboratory Data—On admission the blood diastase was 84, blood sugar 151 mg. Two days after admission cholecystographic examination showed a poorly functioning gallbladder containing questionable calculi. On the night of April 29, 1937, she developed an attack of severe upper right quadrant and epigastric pain radiating to the interscapular region. Temperature 99.6° F, pulse 80, leukocyte count 9,150. The following morning the blood diastase was 1,600, urinary diastase 5,714, blood sugar 269. By May 1, 1937, the symptoms had subsided and the patient was discharged. No further diastase determinations were made.

This attack, which by most observers would be considered an attack of biliary colic, was probably of pancreatic origin.

Case 17—F. R., male, age 75, was admitted to the City Hospital May 7, 1937, complaining of severe, sharp upper abdominal pain of six hours' duration accompanied

by vomiting. Similar previous attacks had occurred during the preceding seven months, during which time roentgenologic examination of the gallbladder gave inconstant findings. Temperature 99.6° F, pulse 100, leukocyte count 15,800.

Examination showed the entire upper abdomen, particularly the epigastrium, to be extremely tender. Muscle guard was noticed only in the epigastrium. *Laboratory Data*—The blood diastase values in the morning and afternoon were respectively 1,200 and 918, urinary diastase 8,040. The icterus index was 50, blood sugar 109 mg. During the following few days there was a gradual improvement in symptoms and signs. By May 10, 1937, the blood diastase had dropped to 150 and the following day to 120. The icterus index was then 60. The gallbladder was not visualized on cholecystography. The patient was discharged May 22, 1937.

Case 18—A G, female, age 65, was admitted to the Jewish Hospital May 10, 1937, 36 hours after the onset of an attack of severe, generalized abdominal pain accompanied by vomiting. The pain persisted as an intense aching, interrupted at frequent intervals by knife-like thrusts in the epigastrium. Temperature 100.4° F, pulse 96, leukocyte count 22,450.

Examination elicited extreme tenderness and moderate rigidity in the epigastrium and upper right quadrant, the rest of the abdomen was less tender. *Laboratory Data*—The blood diastase on admission was 1,778, blood sugar 109 mg. The following day there was much symptomatic improvement but upper abdominal tenderness persisted. The blood diastase fell to 376, and the urinary diastase was 4,286. The abdominal symptoms had entirely subsided by May 14, 1937. The following day there was an elevation of temperature and pulse, and the patient complained of pain and dyspnea. Signs of fluid in the chest were found and roentgenologic examination showed a bilateral hydrothorax. This gradually cleared up spontaneously. Cholecystograms, May 19, 1937, showed poor gallbladder visualization. By May 21, 1937, the blood diastase had fallen to 278, and the urinary diastase to 800, on May 24, 1937, the blood diastase was 147. The patient was discharged May 26, 1937.

Case 19—H P, male, age 65, was admitted to the City Hospital June 29, 1937, six hours after the onset of an attack of excruciating upper abdominal pain which bore little resemblance to his previous epigastric discomfort. It began, just before the time for his evening meal, as an aching pain, and within two hours had become so sharp and penetrating that it caused him to "double up." Vomiting had occurred once. An attack of similar nature was recalled as having occurred two years previously. Temperature 99.6° F, pulse 80, leukocyte count 7,100. The patient gave a history suggestive of the presence of a peptic ulcer of at least eight months' duration, characterized by a gnawing epigastric pain coming on one-half to one hour after each meal, which could always be relieved by the ingestion of food or alkalis.

Examination elicited marked tenderness of the entire upper abdomen, particularly the epigastrium. A tentative diagnosis of perforated peptic ulcer was made, but roentgenologic examination showed no evidence of pneumoperitoneum. *Laboratory Data*—Blood and urinary diastase determinations, soon after admission, gave values respectively of 2,400 and 24,000, blood sugar 158 mg. That afternoon the blood diastase was 3,000. The following day there was considerable improvement in symptoms. Moderate epigastric tenderness was still present, but no rigidity was noted. The blood diastase had fallen to 990. By July 2, 1937, the symptoms had completely subsided and the blood diastase had fallen to 120. Gastro-intestinal and cholecystographic roentgenograms showed no abnormal findings. The patient was discharged July 9, 1937.

Although the suggestive ulcer history cannot be completely disregarded in this case, the present attack resembled most closely one of transient acute pancreatitis. We are of the opinion that the diastase determinations saved this patient from a celiotomy.

Case 20.—B S, female, age 66, was admitted to the Jewish Hospital September 20, 1937, ten hours after the onset of an attack of sudden, severe generalized abdominal pain mostly localizing in the upper right quadrant and epigastrium. Vomiting had occurred once. Temperature 99.4° F, pulse 88, leukocyte count 19,300.

Examination elicited diffuse abdominal tenderness and rigidity, which was most marked in the epigastrium and upper right quadrant. Roentgenologic examination showed no evidence of subdiaphragmatic air or intestinal patterning. *Laboratory Data* Blood and urinary diastase determinations were respectively 3,780 and 12,500. The following day there was considerable symptomatic relief, but tenderness in the upper right quadrant persisted. At that time the blood diastase was 2,370, blood sugar 88 mg, icterus index 15. On September 23, 1937, the blood diastase fell to 226, and the pain had completely subsided. On September 27, 1937, the patient developed another attack of a similar but less severe nature, and some jaundice was noted. The following day the jaundice was more intense, and the icteric index was 40. The blood diastase showed an increase to 985. By September 30, 1937, the second attack had subsided, the jaundice disappeared, the blood diastase had fallen to 180. The patient was discharged.

Case 21.—E L, male, age 33, was admitted to the Jewish Hospital November 17, 1937, for study following a series of attacks of upper abdominal pain suggestive of gallbladder disease. Two months previously the blood diastase had been normal. The day before admission some jaundice was noted. Cholecystograms revealed a poorly outlined gallbladder with questionable calculi. The day after admission the patient developed an attack of moderately severe, sharp epigastric and upper right quadrant pain. The temperature and pulse were normal, leukocyte count 12,000.

Laboratory Data—The blood diastase was 1,113. By November 19, 1937, the attack had subsided, and the blood diastase had fallen to 169. The patient was discharged November 23, 1937.

The clinical features of the cases cited are not sufficiently distinctive at the time of admission to suggest readily a diagnosis of transient acute pancreatitis. Most characteristically the attack begins with sudden, severe upper abdominal pain radiating at times to a corresponding area on the back or to either shoulder. Nausea or vomiting may or may not be present. Depending upon the severity of the attack, signs of shock may be demonstrable. Occasionally there is a history of similar previous attacks. Examination usually reveals marked tenderness of the upper abdomen and rigidity of varying degrees. Early in the attack the temperature and pulse are usually normal, later they may be elevated. The leukocyte count is usually high. It can readily be seen that such a picture, one which may accompany several upper abdominal and even extra-abdominal disorders, is hardly conducive to more than consideration of the possibility of acute pancreatitis. One must, therefore, rely upon laboratory studies to help establish a diagnosis.

Such tests as the adienalin-mydiastasis test^{20, 21, 22} of Loewi, examination of the pancreatic ferments by intubation of the duodenum,^{24, 18, 23, 25} determination of the lipase in the blood stream,^{26, 24, 18, 28, 27, 30, 25, 13} and of trypsin in the stool,^{24, 18} examination of the fat contents of stool after ingestion of a test meal,²⁴ have given inconstant values, proven too slow of determination or impossible to perform on a patient so acutely ill.

Blood and Urinary Diastase—The presence of diastase in the circulating blood and in the urine has been known for many years. There has accumu-

lated in the literature particularly during the last 35 years a mass of experimental data and clinical observations on diastase, much of which presents conflicting and confusing results and opinions. Many of the contradictory results of the earlier investigations, upon the origin and significance of the diastase, were probably due to differences and inaccuracies in the methods of determination, and should, therefore, be accepted only after thorough deliberation. Most investigators have now adopted the starch-sugar reduction method first performed on dogs by Kaufmann,²⁹ and on man by Moeckel and Rost,³¹ and thereafter frequently modified. Even with a standardization and simplification of procedure, variability in starch preparations resulted in some errors in diastase determination. The use of soluble starch is one cause of conflicting results, since soluble starch shows great variations in composition, and, as a consequence, different starch preparations give different results with the same amount of diastase. The main source of errors in the older methods, according to Somogyi,^{10, 32} is failure to recognize the kinetic laws of enzymatic reaction. In Somogyi's method, which we have used in our diastase determinations, due consideration is given to these factors, and one obtains consistent and reproducible results. Normal blood diastase values obtained with this method range between 80 and 180, meaning that 1,000 cc of blood plasma incubated with starch for 30 minutes, under standard conditions, produce reducing substances that reduce as much copper as 80 to 180 mg of glucose.

Diastase in Pancreatic Involvement—Wohlgemuth³³ pointed out that the diastatic activity of the urine was increased in acute pancreatic disorders. Similar increases during pancreatic disorders in the urinary or blood diastase, or both, have been obtained by many investigators, including Hirschberg,³⁴ Benézui,³⁵ Marino,³⁶ Lindemann,³⁷ Katsch,¹⁸ Elman,³⁸ Elman, Aineson, and Graham,³⁹ Popper,⁴⁰ Beinhart,⁴¹ Mushin,⁴² Rost,⁴³ Briansteanu and Boutroux,⁴⁴ Foged,⁴⁵ Henderson and King,⁴⁶ Vianna,¹⁰ Mahner,¹³ and Trasoff and Scarf.⁴⁷ Increased diastatic activity has also been obtained in experimental acute pancreatitis produced by injecting, without pressure into the pancreatic ducts, a variety of chemicals, bacterial suspensions, and bile.^{2, 9, 48} Further confirmatory evidence that the pancreas is involved in the production of diastase was obtained by ligation of the pancreatic ducts,^{49, 50, 51, 52, 53, 54, 55} which procedure practically uniformly resulted in a rapid rise of the blood diastase lasting several days after which there was a return to normal. Similarly, experimentally induced trauma to the pancreas has resulted in increased diastase values.^{56, 52, 57, 55} That the rise of blood diastase following ligation of the pancreatic ducts is due to a backing up of the ferment and absorption into the blood stream, and the subsequent fall consequent to atrophy of the secreting cells seems quite certain.^{49, 50} The rise associated with trauma of the pancreas is probably the result of destruction of acinar membranes, diffusion of diastase into the interstitial tissue, and absorption into the blood stream. It is very likely that the rise associated with acute pan-

creatitis is due to a combination of these factors, inflammatory or spastic occlusion to the duct system and interstitial absorption of diastase

That the pancreas is not the sole source of blood diastase seems reasonably certain. Complete pancreatectomy does not result in a permanent absence of circulating diastase. On the contrary, after an initial drop in the diastase following pancreatectomy there is usually a return to normal or slightly subnormal levels^{58, 59, 50, 52, 60, 61, 62}. Some investigators^{63, 64} have found little or no change following pancreatectomy, others^{65, 66} have found even an increase. Furthermore, atrophic changes in the secreting cells following ligation of the pancreatic ducts are not accompanied by a permanent, and seldom by a temporary, decrease in the diastase^{51, 48, 55}. Considerable evidence, discussion of which is out of the scope of this paper, has accumulated to consider the liver and muscle tissue as the possible additional source of circulating diastase. The pancreatic diastase (as well as lipase and trypsin) seems to enter the blood stream only after certain damages to the gland, such as acute inflammation and trauma.

For practical purposes we may conclude that normal individuals maintain a fairly constant level of blood diastase,^{67, 24, 19, 55} that different individuals show variations of as much as 100 per cent within the normal limits,^{35, 52, 68, 69, 19} that diastase is excreted in the urine with little diurnal variation,^{70, 67, 24, 52} that physiologic functions, such as food ingestion, exercise, and sleep, have little effect on the diastatic values of the blood,^{63, 65, 67, 71, 66, 72, 73} that the blood-urine diastatic ratio is quite constant except when the renal function is deranged, in which case the blood diastase is increased and the urinary diastase decreased or unchanged,^{74, 75, 24, 76, 72, 77, 44} that following a rise in the blood diastase, unless there is an impairment of kidney function, there results in two to five hours a corresponding rise in the urinary diastase^{54, 24, 72}.

Importance of Diastase in Diagnosis of Acute Pancreatitis—Since blood diastase values remain so constant in normal individuals, the sudden marked rise associated with acute pancreatic disease is highly significant. Unger and Huess,⁷⁸ Walzel,¹⁷ Kaczander,⁷⁹ Beinhard,⁸⁰ Peterson,⁸¹ and Mahner¹³ have expressed the belief that elevated diastase values are always indicative of acute pancreatic disease. With this statement we can agree, provided that a clinical picture resembling acute pancreatitis is associated. During routine diastase determinations on several hundred admissions to the Jewish Hospital, we have noted a few persistently high diastase values without obvious cause. High blood diastase values have also been obtained in cases of renal impairment. Furthermore, our records reveal several high diastase values in cases of peptic ulcer perforating acutely into the pancreas¹¹⁴. Excepting perforations of this type, in no other common condition confusable with acute pancreatitis, has there been demonstrated an increase in the blood diastase. Our many diastase determinations lead us to conclude that repeated normal blood diastase determinations made early during the height of an attack of acute upper abdominal pain exclude the pancreas from consideration. We make this statement with the full knowledge that there have been

three isolated reports of single cases of acute pancreatitis accompanied by normal urinary diastase values,^{82, 45 13} in none of these cases was the diagnosis confirmed by tissue examination, nor was the absence or presence of renal impairment mentioned.

The usefulness of diastase determinations in helping to establish a diagnosis of acute transient disease of the pancreas can be impaired if one is not careful to make early and repeated determinations. Foged⁴⁵ and Elman⁷ have pointed out that as early as 36 hours after the onset of an attack of acute pancreatitis, and almost simultaneously with the disappearance of symptoms, the blood diastase may revert to normal. Our experience has been similar (Cases 1, 3, 5, 8, 11). Most clinics are familiar with cases which are admitted as emergencies, presenting symptoms and signs of acute upper abdominal lesions which rapidly clear up. At times they leave the hospital without a diagnosis having been made. Sometimes they are uncertainly or incorrectly diagnosed acute intestinal obstruction, biliary tract colic, perforating peptic ulcer, acute appendicitis or coronary disease. If early blood diastase determinations were made on cases of this type, it is very likely that a number would show elevated diastase values, thereby directing attention to the pancreas. We are of the opinion that the rôle of the pancreas in the production of epigastric pain has been frequently disregarded. The importance of daily, and sometimes twice daily, determinations can hardly be overestimated. Subsequent values reflect on the progression or retrogression of the attack.

Most investigators have made it a matter of personal choice as to whether diastase determinations should be made on the blood or on the urine. Of course, it would be preferable to do both, but frequently this is impractical. When there is a choice, blood determinations are preferable for several reasons. Normal blood diastase fluctuates less widely than normal urinary diastase. The latter varies between 200 and 800 and shows considerable irregular diurnal variation. Furthermore, derangement of renal function, undetected during an emergency, might mask the approximate level of the circulating diastase. On the other hand, since the urinary diastase follows fluctuations in the blood by a lag of several hours, urinary diastase determinations may furnish valuable information if made during the subsidence of an attack. In this condition the urinary diastase may remain elevated after the blood diastase return to normal. Case 10 is an example of the importance of urinary diastase determinations during the subsidence of an attack.

There seems to be no constant relationship in our cases between the severity of an attack and the level of diastatic activity. For example, Case 6 which was only of moderate severity had a maximum diastase of 2,000, while Case 4 which presented very severe symptoms had a maximum diastase of 400. These findings are in agreement with those of Walzel,¹⁷ Pribram,⁸³ and Mahner.¹³ They may be best explained by presuming that the determinations were made during different stages of the attack. The histories of our cases do not clarify this point.

Relation to Disease of Biliary Tract—It is a fact that many cases of acute pancreatitis present signs and symptoms of precedent or concurrent biliary tract disease^{1, 15, 84, 2, 85, 86, 4, 87, 9, 88, 89, 90, 91, 46, 7, 25} At least half of our cases presented unmistakable signs of biliary tract disease, and several more have given presumptive evidence of this relationship. On the surface, this association would seem to confuse the differential diagnosis. Nevertheless, biliary tract disease *per se* is not accompanied by an elevated blood diastase. On the contrary, many cases of biliary tract disease when associated with impaired liver function present, according to Somogyi,¹⁹ subnormal diastase values. This observation has been so constant, that in our laboratory the blood diastase has attained somewhat the status of a liver function test.⁴ Since the majority of the cases of acute pancreatitis have some relationship to biliary tract disease, one would expect to find at times evidence of impaired liver function. Unfortunately the diastase increases that occur in acute pancreatitis are of such magnitude as to cover up completely the decrease that might result from the concurrent impairment of liver function. The decreased carbohydrate tolerance which occasionally occurs in these cases furnishes additional evidence of liver impairment. We are of the opinion that when a patient with biliary tract disease suddenly develops an elevated blood diastase one should be highly suspicious of the presence of pancreatic involvement.

Carbohydrate Tolerance—Several investigators have noted that acute pancreatitis is frequently associated with hyperglycemia and glycosuria.^{1, 2, 92, 3, 41, 93, 94, 95, 98} But many cases of acute pancreatitis occur without glycosuria. Henderson and King⁴⁶ noted glycosuria in only four of 60 cases, Love²¹ in three of 30 cases, Walzel¹⁷ in 10 per cent of his cases, and Elman⁴ in six of 37 cases. DeKlimko²⁵ found an absence of reducing sugar in the urine of 19 cases. Vianna¹⁰ thought glycosuria was a rare occurrence. We have made blood sugar determinations on all our cases. While an increase has been noted in several instances, it has not occurred with sufficient frequency to ascribe great significance to it. The emergency nature of many of these cases renders the securing of a fasting blood specimen at times impracticable. While we do not consider it an indispensable part of our diagnostic armamentarium, we recommend that a blood sugar determination be made, since it may add weight to one's diagnostic conclusions. It is interesting to speculate on the causation of hyperglycemia in acute pancreatitis. It is generally assumed that it results from a temporary dysfunction of the islands of Langerhans and consequent diminution of insulin. Brocq and Varangot⁹⁴ thought that some of the insulin was destroyed by trypsin. Against these hypotheses is the well known observation that many cases of acute pancreatitis can proceed to complete necrosis of the gland without the occurrence of hyperglycemia. We are of the opinion that a more tenable assumption

⁴ Studies are now being made combining the simultaneous performance of hippuric acid and diastase tests.

would be the decrease of carbohydrate tolerance resulting from the associated impairment of liver function

Treatment—Once a diagnosis of acute pancreatitis has been considered likely, it is very dubious if the first examination will distinguish between a pancreatitis of the transient type or one which will progress to necrosis with its accompanying high mortality. The question will then arise as to whether the patient should be treated expectantly in an endeavor to establish a more accurate diagnosis or whether immediate operation should be performed. This question cannot be answered with certainty for it evokes a discussion of the highly controversial problem of the therapy of acute pancreatitis. For many years it has been the custom to operate as soon as a diagnosis of acute pancreatitis was considered even questionably tenable. It was well known that acute pancreatitis of the hemorrhagic, necrotic or suppurative types has been fraught with an extremely high mortality rate. Any procedure that offered the slightest chance of reducing this mortality rate was eagerly embraced. Because evidence greatly favored the theory of reflux of bile into the pancreatic ducts as the main etiologic agent of acute pancreatitis,^{96, 15 3, 85 97 98} such operative procedures as cholecystostomy, choledochostomy, cholecystectomy, and combined cholecystectomy and choledochostomy were advocated to decompress the biliary tract. Some surgeons advocated incision and drainage of the capsule of the pancreas, or of the gland itself, to relieve tension and to remove the products and cause of autodigestion. Others combined biliary decompression with pancreatic or lesser peritoneal cavity drainage. Using these procedures Koster and Kasman⁹⁹ reported a mortality rate of 22.7 per cent in 22 cases, and Quick⁸⁶ of 38.1 per cent. Brocq⁹⁵ noted a reduction of mortality rate from 78 per cent, before 1910, to 67 per cent, since 1910. Schmieden and Sebening,¹⁵ and McWhorter⁸⁵ reported lower mortality rates in early operated cases than in unoperated cases. Other observers favoring early operative intervention are Zoepffel,¹ Waring and Griffiths,²² Chamberlain,¹⁰⁰ Oehler,¹⁰¹ Stetten,³ Tammann,⁹² Kappis,¹⁰² Thomas,¹⁰³ Penin,⁶ and May.¹²

Serious objections have been raised to the principles forming the basis for early operative treatment. While many observations attest to the relationship of biliary tract disease to acute pancreatitis, its exact nature is not known. Many cases of acute pancreatitis have been shown to have neither the anatomic configuration of the pancreatic and common bile ducts generally associated with these cases,^{85 104 89 9 91} nor the clinical findings suggestive of an associated biliary tract disease (Cases 4, 5, 13, 14). Hofhauser (cited by DeKlimko²⁵) has even implanted the pancreatic duct into the gallbladder without causing acute pancreatic disease. Furthermore, it is doubtful if drainage of the biliary tract could result in establishing patency in a pancreatic duct system already impaired by an edematous or inflammatory process. Drainage of the pancreas by incision of the capsule, or of the gland itself, can hardly be expected to arrest the process of acute pancreatitis. Nordmann¹⁴ reported several cases, observed both at early operation and at autopsy, that progressed

to complete gland necrosis in spite of what he considered to be adequate biliary and pancreatic drainage Walzel,^{105, 17} Mikkelsen,¹⁰⁶ Douglas,¹⁰⁷ and Telford⁹⁷ have expressed beliefs that pancreatic drainage may further damage an already severely compromised gland, may result in severe hemorrhage, promote massive slough of the gland, or may, if the patient survives, establish a pancreatic fistula Walzel¹⁰⁵ was emphatic in condemning operative interference, he felt that acute pancreatic necrosis was not a bacterial necrotic focus that could be arrested by incision and drainage but purely a chemico-biologic process Smead¹⁰⁸ thought that operation not only did not relieve the cause of shock but also added greatly to the seriousness of the case Leveuf,¹⁶ Grégoire,¹⁰⁹ and Monoud and Doi,¹¹ while admitting that operation might be necessary to establish an adequate diagnosis, were skeptical of its offering anything from the standpoint of cure Several investigators favoring early operative procedures did not submit their most acutely ill or moribund patients to operation The mortality figures for their conservatively treated cases were, accordingly, abnormally high Even those investigators favoring early operative intervention at times reported high mortality rates For example, Oehler,¹⁰¹ Tammann,⁹² and Biocq⁹⁵ reported mortality rates of 58, 55, and 67 per cent respectively In the hands of other investigators results of early operative treatment bordered on the disastrous Eliason and North¹¹⁰ reported a mortality rate of 80 per cent in their cases, Henderson and King⁴⁶ of 50 per cent, Nordmann¹⁴ of 52 per cent, and Trasoff and Scarf⁴⁷ of 75 per cent One is forced to conclude that the results of early operative intervention are highly unsatisfactory At best the recovery rate in acute pancreatic necrosis averages no more than 50 per cent Nor does the type of operation seem to influence the ultimate result

More conservative measures have, accordingly, been adopted by many investigators These have varied from operation as soon as signs of shock have largely abated to completely nonoperative procedures Koite,¹¹² Walzel,¹⁷ Nordmann,¹⁴ Eliason and North,¹¹⁰ deTakats and Mackenzie,⁹³ Bernhard,⁸⁰ Peterson,⁸¹ Hoime,⁸⁸ Henderson and King,⁴⁶ Johns,⁹¹ Smead,¹⁰⁸ and deKlimko²⁵ favored conservative treatment during the period of acute symptoms, followed by operative exploration of the biliary tract when the acute symptoms had subsided Mikkelsen,¹⁰⁶ Felsenreich,¹¹³ Rowland,²⁰ Parry and Murray,⁸⁹ Einhorn,²³ Douglas,¹⁰⁷ Mahner,¹³ and Trasoff and Scarf⁴⁷ were even more conservative, advocating either no operation at all or operating at a later date only if biliary tract disease could be demonstrated The results with more conservative measures, still far from a solution of the problem, have been more gratifying Eliason and North¹¹⁰ reported no mortality in their conservatively treated cases, Smead¹⁰⁸ a mortality rate of 7.5 per cent, Nordmann¹⁴ of 22 per cent, and Mikkelsen¹⁰⁶ of 7.5 per cent

A thorough review of the literature, and a careful consideration of our cases, have convinced us that, until more specific measures are forthcoming to combat acute pancreatic disease, the best results will be obtained by conservative management of all cases This applies not only to lesions of a transient

TABLE I
RESUMÉ OF 21 CASES OF PRESUMPTIVE, TRANSIENT ACUTE PANCREATITIS

Case	In Hospital	Sex	Age	Onset Before Admission	Pain	Vomiting	Jaundice	Tenderness	Rigidity	Leukocyte Count	Blood Diastase*	Urinary Diastase†	Blood Sugar†	Biliary Tract Disease	Remarks
1	5/10/35	I	15	1 day	Upper abdomen	++++	+++	Upper abdomen	++	12,000	5/10/35 1,500 5/11/35 168		5/11/35 74	Present	Operated 5/26/35 and microscopically normal
	6/2/35				++++			++++							
2	6/11/35	I	31	1 day	Epigastric and R U Q radiating to midback	++	+	Epigastric and R U Q	+	12,600	5/22/35 708 5/24/35 100		5/22/35 84 5/24/35 84	Present	Cholecystectomy and choledochostomy 4/25/35 No mention of pancreas Postop blood diastase 66
	6/29/35				++++			++++					12/4/35 99	Present	
3	12/2/35	M	69	1 day	Epigastric and R U Q	++	+++	Epigastric and R U Q	+	24,200	12/4/35 600 12/5/35 150				Exploratory celotomy performed several months before for similar attack, suspected perforated ulcer Negative findings
	12/8/35				++			++					6/5/36 70 6/8/36 154	No evidence	
4	6/5/36	M	60	12 hrs	Epigastric	+	o	Epigastric	++	30,000	6/6/36 400 6/8/36 66				
	6/11/36				++++			++					2/18/36 1,250 2/19/36 136 2/21/36 100	No evidence	
5	2/17/36	M	50	5 hrs	Generalized abdomen	++++	o	Epigastric and R U Q	+	16,000					
	2/21/36				++++			++					9/12/36 2,000 9/13/36 600 600	?	Left hospital before could be worked up
6	9/11/36	I	56	3 days	Epigastric and L U Q	++	+	Epigastric and L U Q	++	7,550	9/18/36 750 9/19/36 666 9/21/36 132 9/23/36 132		9/10/36 120	Intolerant to fat	Chronic alcoholism Intoxicated at onset of attack Associated toxic hepatitis
	9/13/36				++			++					10/20/36 103	?	Left hospital before could be worked up
7	9/18/36				Epigastric		+	Epigastric	++	13,000					
	10/1/36	M	17	5 days(?)	++++	o	+	++++	++						
8	10/19/36	M	68	1 day	Generalized abdomen	++	+	Epigastric and R U Q	+	14,500	10/20/36 600 10/21/36 180				
					+++			++					2/19/36 86	Present	2/20/36 normal sugar tolerance curve
	2/18/36				Epigastric radiating to interscapular region		+	Epigastric and R U Q	++	12,000	2/19/36 1,150 2/20/36 250		1,250		
	2/20/36			1 day			o	R U Q							

TABLE I (Concluded)

Case	In Hospital	Sex	Age	Onset Before Admission	Pain	Vomiting	Jaundice	Tenderness	Rigidity	Leukocyte Count	Blood Diastase*	Urinary Diastase*	Blood Sugar†	Biliary Tract Disease	Remarks
17	5/7/37 5/22/37	M	75	6 hrs	Epigastric ++++	++	+	Upper abdomen ++++	+++	15,800	5/8/37 1,200 5/10/37 150 5/12/37 120	5/8/37 8,040	5/8/37 109	Present	
18	5/10/37 5/26/37	F	65	36 hrs	Epigastric ++++	++	o	Upper abdomen ++++	R U Q +++	22,450	5/10/37 1,778 5/11/37 376 5/21/37 278 5/24/37 247	5/11/37 4,286 5/21/37 893 800	5/10/37 109	No evidence	
19	6/29/37 7/9/37	M	65	7 hrs	Epigastric ++++	+	o	Upper abdomen ++++	++	7,100	6/29/37 2,400 6/30/37 990 7/2/37 120	6/29/37 24,000	6/29/37 158	No evidence	Suggestive previous ulcer history
20	9/30/37 9/30/37	F	66	10 hrs	Generalized abdomen +++ Attack Epigastric and began in R U Q hospital	+	o	Upper abdomen Epigastric and R U Q ++	+++	19,300	9/20/37 3,780 9/21/37 2,370 9/23/37 226	9/20/37 12,500	9/21/37 88 9/23/37 74	Present	Observed during two attacks during this admission
21	11/17/37 11/23/37	M	33	Attack began in hospital	Epigastric and R U Q +++	o	o	Epigastric ++	o	12,000	11/18/37 1,113 11/19/37 169		11/18/37 92	Present	

* Determined by Somogyi's method Normal values 80 to 180

† True sugar values Normal 80 to 100 mg

nature, but also to the more severe lesions of hemorrhage, suppuration and necrosis, from which many succumb regardless of the form of treatment. We have not been convinced that any operative procedure has lowered the mortality rate in acute pancreatitis of any type. While admitting that occasional abdominal exploration may become necessary to help establish a differential diagnosis, the careful use of diastase determinations should reduce the number of explorations to a minimum. If, on operation, evidence of acute pancreatic involvement is found, we are in favor of immediate closure of the abdomen without further interference. We believe that eradication of biliary tract disease should be delayed until the attack of acute pancreatitis has completely subsided. If death should ensue in the meanwhile, we are convinced that no operative procedure would have altered the ultimate result, but, on the contrary, might have hastened it. As additional evidence against early operative treatment we cite our cases of acute pancreatitis. The invariable recovery of these cases under expectant treatment we feel is further argument against operative interference in any case of acute pancreatitis.

CONCLUSIONS

Twenty-one cases of presumptive, transient acute pancreatitis are detailed.

The pancreas is a frequent source of acute upper abdominal pain often attributed to other upper abdominal disorders.

The examination, by newer methods, of the blood and urine for diastatic ferments, if performed early and repeatedly during an attack of acute upper abdominal pain, may furnish valuable assistance in establishing or excluding a diagnosis of acute pancreatitis.

Conservative management seems indicated in all types of acute pancreatitis during the acute stage. Surgical treatment of associated biliary tract lesions should be delayed until the attack of acute pancreatitis has subsided.

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SURGERY AND DIABETES

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DIABETIC patients, as a class, are not immune from those diseases which require surgical treatment. They may be affected by any of the diseases for which operation commonly is performed. In addition, there are certain diseases, such as cholecystitis and gangrene of the extremities, to which they are even more prone than is the average person. Surgeons no longer hesitate to operate upon patients with diabetes, as is proved by the large number of publications on surgical treatment of diabetics in the medical literature of the last decade. Since the advent of insulin, the average surgical mortality rate on diabetic patients has decreased enormously. This has resulted, not only from the use of insulin, but also from clearer understanding of, and improved technic in, the handling of the special problems involved.

Despite the great strides which have been made in the surgical care of diabetic patients, a great deal is yet to be accomplished, as can be seen by noting the wide range of results reported by various investigators. A good many physicians and surgeons, even yet, do not have a full comprehension of the importance of collaboration and team work between the physician and the surgeon, which is necessary if the singular needs of such patients are to be cared for adequately and satisfactorily. For the fact remains that, despite the more optimistic outlook made possible by the decreased mortality rate, an operation upon a diabetic patient is accompanied by more risk than one upon a patient who does not have this disease. Hence it is urgent that an ever-increasing number of surgeons and physicians know how to deal with the emergency presented by the diabetic patient who must be subjected to operation. The fundamental principles of treatment, both before and after operation, can not be stressed too strongly, nor repeated too often.

Surgical Mortality in Diabetes—A glance at Tables I, II, and III shows a great decrease, since the use of insulin, in the death rate following operations upon diabetic patients. Reports published by four authors, both before and since the use of insulin, show that the average mortality rate without insulin was 40.6 per cent, while since insulin has been used, it is 16.0 per cent. This represents a decrease in mortality rate of 57.8 per cent, based on the average of percentage figures, without consideration of the number of cases involved (Table I). Table II shows the results in 2,023 cases reported by various authors, before the advent of insulin. The average mortality rate, calculated on the number of cases, was then 24.2 per cent. In a collective series of 14,231 cases, reported since 1924, the average mortality rate was only 5 per cent, although the range for individual reports was from 1.2 to 68 per cent (Table III). The statistics in these tables show that there has been a marked

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TABLE I
SURGICAL MORTALITY IN DIABETES
Effects of Insulin

Author	Mortality		
	Before Insulin Percentage	After Insulin Percentage	Decrease Percentage
Reed ¹ (summary of other authors)	34.04	12.7	64.6
Saunders ²	62.5	24.5	59.4
Mason ³	22.0	15.0	31.8
Beardwood ⁵	44.0	10.9	75.3
Averages	40.63	16.0	57.8

TABLE II
SURGICAL MORTALITY IN DIABETES
Before Insulin

Series	Cases	Mortality Percentage
Berkman ⁶ (1921)	159	5.0
Lahey ⁷	14	7.1
Berkman ⁸ (1916)	26	7.6
Joslin ⁹ (1919)	61	9.0
Young ¹¹	99	16.1
Cumston ¹²	6	16.6
Joslin ⁹ (before 1917)	27	18.0
Binney ¹³	32	19.0
Karewski ¹⁰	225	21.0
Mason ³	41	22.0
Morrison ¹⁴	775	23.0
Jones ¹⁵	8	25.0
Phillips ¹⁶	101	27.0
Fitz ¹⁷	45	30.0
Strouse ¹⁸	38	31.3
Weeden ¹⁹	160	36.8
Menninger ²⁰	47	42.5
Beardwood ⁵	19	44.0
Fischer ²¹	86	48.4
Saunders ²	24	62.5
Nygind ²²	5	80.0
Gardner ²³	25	80.0
Totals	2,023	24.2

TABLE III
SURGICAL MORTALITY IN DIABETES
With Insulin

Series	Cases	Mortality Percentage
Adams and Wilder ²⁴	327	1 2
Allan ²⁵ (1930)	288	1 7
Bruce ²⁶	97	2 1
Lemann ⁴	43	2 3
Allan ²⁵ (1931)	218	2 7
Bazin ²⁷	73	2 7
Judd, Wilder and Adams ²⁸	667	2 9
Mayo Clinic ²⁹ (combined series from 1921-1932)	7,309	3 3
Elhason ³⁰ (1929-1932)	170	3 5
Elhason ³⁰ (1926)	50	3 6
Menninger ²⁰	22	4 5
John ⁷¹ (1925-1930)	462	4 7
Rabinovitch ³¹	130	5 3
Joslin ³² (1923)	69	5 7
John (1920-1937)	1,273	5 8
Joslin ³³ (1928-1930)	580	5 9
McKittrick ³⁴	1,002	7 6
Weeden ¹⁹	12	8 3
John ⁷¹ (1921-1925)	35	8 5
Roth ³⁵	20	10 0
Joslin ³⁶ (1925)	97	10 3
Beardwood ⁵	91	10 9
McKittrick and Root ³⁷	80	11 2
Foster ³⁸	103	11 6
Petty ³⁹	31	12 6
Joslin ³⁶ (1927)	322	12 7
Law ⁴⁰	15	13 3
Cohen ⁴¹	8	14 0
Joslin ³⁶ (1924)	75	14 6
Joslin ³⁶ (1926)	81	14 8
Mason ³	60	15 0
Ralli and Standard ⁴²	96	16 4
Reed ¹	64	18 7
Coller and Marsh ⁴³	65	24 6
Saunders ²	14	25 4
Bauman ⁴⁴	56	26 7
White ⁴⁵	66	28 7
Carp ⁴⁶	25	35 0
Elhason and Wright ⁴⁷	55	41 8
Apfelbach ⁴⁸		68 0
Totals	14,251	5 0

decrease in the mortality rate in recent years, but they also indicate a tremendous variation in individual reports. This variation is quite difficult to account for, and does not represent merely a difference in the excellence of treatment, but depends also on the type of operation, the type of patient, *i e*, private versus charity patients, and other factors. The difference between the results in major and minor operations in my own cases is shown in Table IV.

TABLE IV
SURGICAL MORTALITY IN DIABETES
(JOHN)

Operations	Mortality Percentage
Major— 983	10.0
Minor— 290	1.7
Total—1,273	5.8

Causes for Decrease in Mortality—Although the use of insulin has been a vitally important factor in the improvement of surgical results in the presence of diabetes, this also is dependent on other factors. Before insulin was available, operations upon a diabetic patient were often performed merely as a measure of last resort, and hence most procedures were of major character.

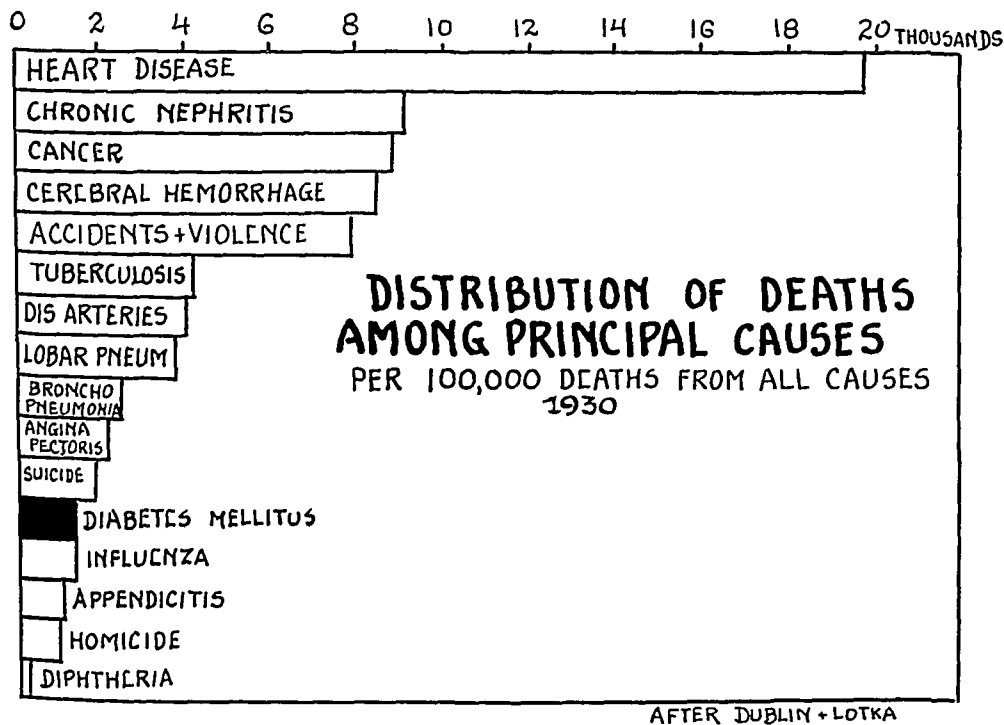


CHART 1 —Leading causes of death

and entailed great risk. The newer anesthetics which are less hazardous have been developed since that time. The proper postoperative and pre-operative care was not so well understood then as it is to-day. All of these factors increased the gravity of the prognosis for a diabetic patient who had

to be operated upon before the era of insulin, and many authorities felt that surgery should not be resorted to, unless it could not possibly be avoided

Increase of Risk in Diabetic Patients—It is not the diabetes *per se* that increases the risk of surgical operations in diabetic patients, for diabetes ranks ninth among the ten leading causes of death (Chart 1). Only 28 persons per 100,000 population die from diabetes, as compared with 261 per 100,000 who die as the result of heart disease. The principal factors which increase the surgical risk in the presence of diabetes are obesity, advanced age, arteriosclerosis and infection.

2000 DIABETICS JOHN

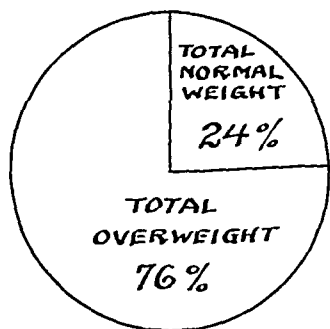


CHART 2—Relative proportion of obesity in diabetic patients

Any obese patient presents a poorer risk surgically than one who is thin. The proportion of stout patients among diabetics is far greater than among nondiabetics, and this naturally increases the number of deaths following operation (Chart 2).

Many operations upon diabetic patients are performed on those of considerable age, for diabetes is preponderantly a disease of advanced years. Chart 3 shows the increased mortality rate in patients more than 50 years of age. Aside from the actual age, diabetic patients are physiologically older than those without diabetes,

because of the effect of the disease on the circulatory system. The approximate physiologic age can be estimated roughly by adding the number of years that diabetes has been present to the patient's actual age. Thus a person age 60, who has had diabetes for 16 years, is approximately 76 years old physiologically.

The resistance of the diabetic patient to infection is always less than that of a normal person, and this presents one of the major risks when the patient is operated upon. Hyperglycemia hinders speedy healing of the tissues, as has been pointed out by McKittick⁵⁰ and by Lewis.⁴⁹ If serious infection develops following an operation, the diabetes may be markedly aggravated, and may even get beyond control.

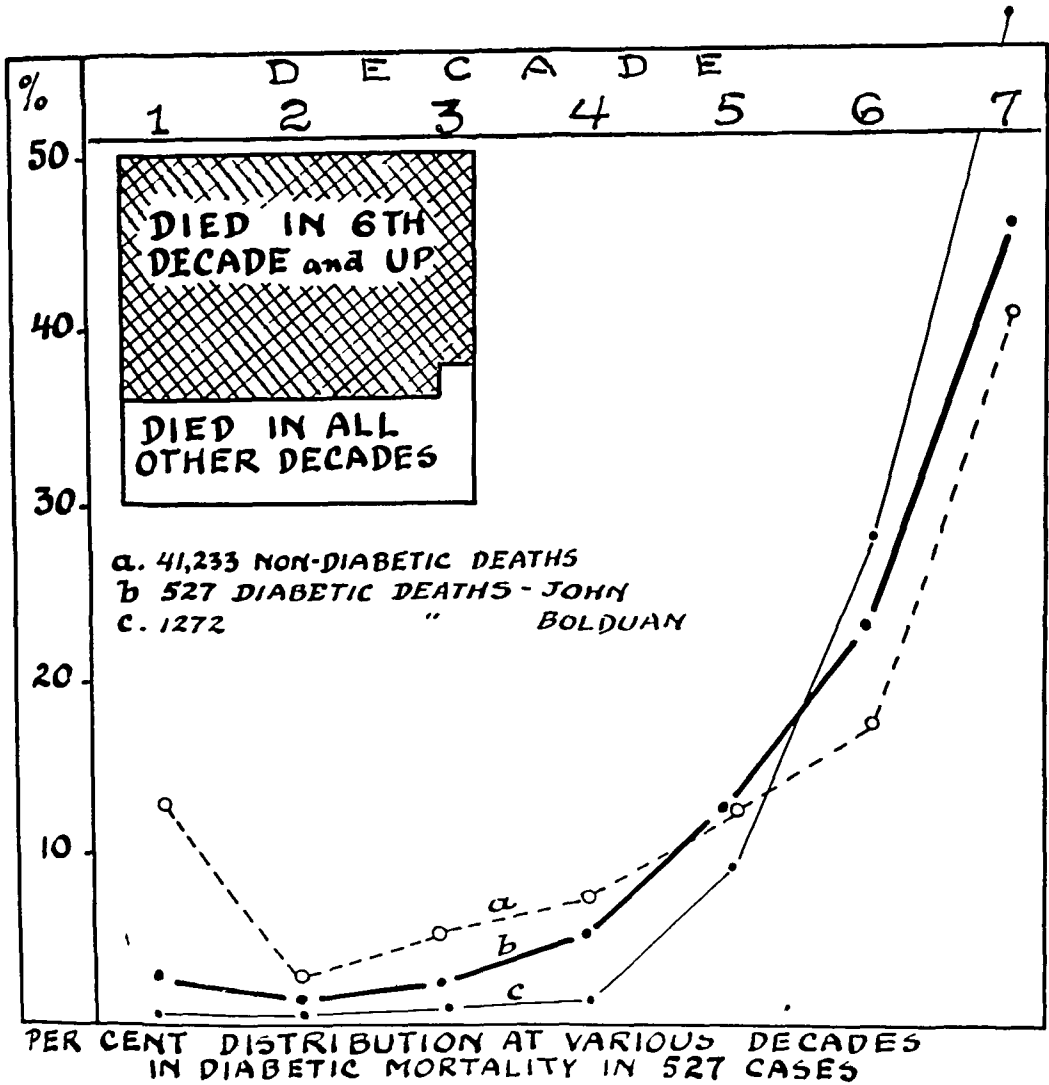
SPECIAL SURGICAL PROBLEMS IN DIABETES—Cholecystitis That an infection of any kind aggravates diabetes is so well known that it requires no comment. While the statistics available do not give any precise picture of the relative proportions of diabetic and nondiabetic patients with gallbladder disease, it is a matter of common experience that diabetic patients are more prone to affections of this organ. The presence of cholecystitis, as based on routine autopsy records, has been reported by some authors as more than 20 per cent. McKittick,³⁷ in a series of 24 diabetic cases, found an incidence of almost 35 per cent. While this series is too small to warrant a general statement, it is probably true that it is indicative of the greater proportion of patients with cholecystitis in diabetic patients.

Even as early as 1910, Mayo Robson⁵¹ pointed out the relation of cholecys-

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titis to diabetes, and stated that in many instances diabetes might be averted by the early removal of the gallbladder Joslin^{12, 13} has stressed this point, too, for many years

Chronic cholecystitis is a mild infection, but still it affects the diabetic state adversely It is extremely common to see marked improvement, with increased sugar tolerance, and marked diminution in the insulin requirement following cholecystectomy (Table V) Hence when a diagnosis of gall-



bladder disease has been made, a diabetic patient can be promised improvement following cholecystectomy This can be performed without undue risk, according to recent records of the results of this operation on diabetic patients In a total of 216 cases, reported by nine authors, the surgical mortality was only 3.3 per cent (Table VA)

Gangrene of the Extremities—Gangrene of the extremities is of common occurrence in diabetic patients, and usually requires surgical treatment This condition, which is commonly called diabetic gangrene, would be more precisely referred to as arteriosclerotic gangrene, for it is of the same type as is seen in nondiabetic patients with arteriosclerosis It is more common, how-

TABLE V

ANALYSES OF PRE- AND POSTOPERATIVE BLOOD SUGAR IN EIGHT CONSECUTIVELY CHOLECYSTECTOMIZED PATIENTS (JOHN)

	Sex	Age	Aver Bl Sug Before Oper *	Insulin Requir	Aver Bl Sug After Oper *	Insulin Requir
Mrs P	F	60	210	45 Units	140	0 Units
Mrs Pe	F	68	190	30 Units	85	0 Units
Mrs La	F	47	190	20 Units	130	0 Units
Mrs Sm	F	59	240	20 Units	160	15 Units
Mrs La	F	50	238	30 Units	92	0 Units
Mr Ke	M	52	200	60 Units	140	40 Units
Mr Be	M	39	190	20 Units	160	15 Units
Mrs Se	F	60	190	40 Units	130	25 Units

* The averages given are those obtained from three blood sugars on a check-up, namely, before breakfast, lunch and dinner, showing the increased degree of sugar tolerance and the lessened amount of insulin required postoperatively following cholecystectomy

TABLE VA

SURGICAL MORTALITY IN DIABETES

Gallbladder Operations

Author	Cases	Mortality Percentage
Bazin ²⁷	10	0
Foster ³⁸	3	0
Joslin ³⁶	13	0
Lemann ⁴	1	0
McKittrick ⁵⁰	59	0
Ralli and Standard ⁴²	2	0
Judd, Wilder, Adams ⁷⁸	40	2 5
John	43	4 6
McKittrick ³⁷	45	8 8
Totals	216	3 3

ever, in diabetic patients because they are more likely to have advanced arteriosclerosis. The occurrence of gangrene is conditioned far more by the vascular state than by the degree of diabetes. If the diabetes were the more important factor, as is still claimed by some authorities, it would be seen more commonly in patients with extremely high levels of blood sugar, who have neglected the proper treatment of the diabetic condition. But it seems that the greater proportion of those who have gangrene have mild diabetes, sometimes of short duration.

The actual incidence of gangrene in diabetes has been reported variously

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as from 2.4 to 18 per cent. The average percentage of thirteen reported series is 5.2 (Table VI). If severe, uncontrolled diabetes were the important etiologic factor, it seems to me that this percentage would be much greater. However, it should be noted that some authors report a disparity in the incidence of gangrene in private and in charity cases. This may be due to neglect of other factors as much as to the lack of control of the diabetes. Gangrene has not decreased appreciably since the use of insulin, and there certainly can be no question that the general attention and care of diabetic patients has improved tremendously during this time.

TABLE VI
INCIDENCE OF GANGRENE IN DIABETES

Author	Cases	Gangrene Percentage
John	4,871	2.4
Mayo Clinic ²⁵	684	2.4
University of Pennsylvania Hospital (before 1923)	355	2.5
Paullin ⁵²	560	2.8
Joslin ⁵³	3,000	3.0
Lemann ⁵⁴ (private cases)	471	5.3
Peter Bent Brigham Hospital ⁵⁴	969	7.0
Massachusetts General Hospital ⁵⁴	600	9.0
University of Pennsylvania Hospital (since 1923)	845	6.2
Tuoro Infirmary ⁵⁴ (private cases)	201	10.0
Boston City Hospital ⁵⁴	967	11.2
Philadelphia General Hospital	1,305	13.0
Lemann ⁵⁴ (charity cases)	439	18.0

The answer to the question of why there are varying degrees of arteriosclerosis in diabetic patients, whether well cared for or not, certainly has not yet been found. Since we do not know the cause of increasing arteriosclerosis, the best we can do is to make an effort to recognize the premonitory symptoms of circulatory insufficiency as early as possible, and thus to try to prevent the development of gangrene. A sensation of cold and pain in the feet, cramps in the calves of the legs, especially when lying down at night, are the first symptoms.

It has been pointed out by Starr⁵⁵ and others⁵⁶ that a considerable reduction in the peripheral circulation may occur without the development of any physical signs. On the other hand, the latter has also shown that the minute vessels may demonstrate normal responses even when the physical examination reveals gross evidence of arterial sclerosis. Starr has used histamine tests to detect the actual changes in the circulatory response. One-half of the diabetic patients he tested in this manner showed diminished circulatory

responses in the feet, and in 34 per cent this impairment was extreme. He asserts that the preponderant proportion of patients with gangrene are included in this latter group. Gangrene develops only when the reduction in circulation is of advanced degree.

The preventive treatment of diabetic gangrene is all aimed at stimulation of the circulation in the extremities. Among the measures which have been advocated are hot foot baths at night, contrast baths, woolen bed socks, and the positive-negative pressure pump. In the application of heat, care must be taken to prevent burning. Joslin³⁶ has also stressed particularly the cleanliness of the feet. Another important factor is extreme caution in cutting the toe nails, to prevent even a small injury which may not heal.

There is some controversy as to the efficacy of the leg pump in stimulating circulation. Some authorities, especially McKittrick,³⁴ have asserted that it is of no value when gangrene is already present. On the other hand, I have been impressed with the results in some cases of this type, for some feet have been saved which I am sure would have had to be amputated without the aid of this appliance. The contraindications to its use are (1) Moist gangrene or spreading infection, (2) lymphangitis, (3) thrombophlebitis, (4) varicose veins, and (5) cardiac decompensation with edema.

TABLE VII
MAJOR AMPUTATIONS IN DIABETES

Author	Cases	Mortality Percentage
Maes ⁵⁷	60	5 0
Judd, Wilder, Adams ²⁸	15	6 6
Walters, Meyerding, Judd, Wilder ²⁹	86	11 0
McKittrick ³⁷	365	13 9
John	61	16 0
Foster ³⁸	31	19 0
Young ¹¹	19	21 0
Bothe ⁵⁸	60	22 0
Saunders ⁹	25	24 0
Joslin ³⁶	56	27 0
Ralli and Standard ⁴²	36	33 0
Smith ⁵⁹	18	34 0
Reed ¹	13	38 0
Coley ⁶⁰	10	40 0
Eliaeson ³⁰		56 0
Apfelbach ⁴⁸		65 0

The mortality rate from amputations for gangrene ranges from 5 to 65 per cent (Table VII). Most of the high rates were reported by general hospitals whose patients represented poor risks because of lack of previous care and an advanced condition of the gangrene. Various factors affect the mortality rate in these cases. These include the type of infection, the age of

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the patient, the degree of shock, and the degree of regulation of the metabolic disorder. When one considers the shock occasioned by an extensive amputation and the advanced age of most of these patients (Table VIII) it is easy to see why the mortality rate following this type of operation is higher than in many other conditions.

TABLE VIII
THE AGE AT ONSET OF DIABETIC GANGRENE

Author	Average Age
Bothe ⁵⁸	51
Lewis ⁶¹	54
Ehason and Wright ⁴⁷ (1926)	59.2
Joslin ³⁵ (1923)	61
Ehason ³⁰ (1932)	61.6
McKittrick and Root ³⁷ (1928)	64.9
Ehason and Wright ³⁰ (1931)	69.9

TABLE IX
SURGICAL MORTALITY IN DIABETES
Various Surgeons

Surgeon	Operations	Mortality Percentage
1	8	0
2	3	0
3	9	0
4	7	0
5	9	0
6	4	0
7	59	3
8	232	5
9	17	6
10	48	6
11	49	6
12	12	8
13	82	17

Collaboration of Internist and Surgeon—Operation upon a diabetic patient presents a problem which requires the combined talents of an internist and a surgeon who are especially interested in diabetes. The published results attest to the importance of this collaboration. The best results come from perfect team work. A glance at the records from the Mayo Clinic, where such service and team work are highly organized, shows that the surgical mortality in diabetic patients is consistently low. In 1924, they²⁴ reported 327 operations upon diabetic patients with a death rate of 1.2 per cent, in

1930, 288 operations, with 17 per cent, in 1931, 218 operations with 27 per cent fatalities²⁵

These results should be encouraging to everyone interested in the problem of surgery and diabetes, for they show what can be accomplished when there is the proper interest and coordination of effort

Citing from my own experience some records to show the importance of collaboration of surgeon and internist, which means the proper care of the diabetic patient, the recommended measures were taken before and after operation, but one surgeon refused to recognize the importance of these procedures and would not wait until the patient was deemed ready for the

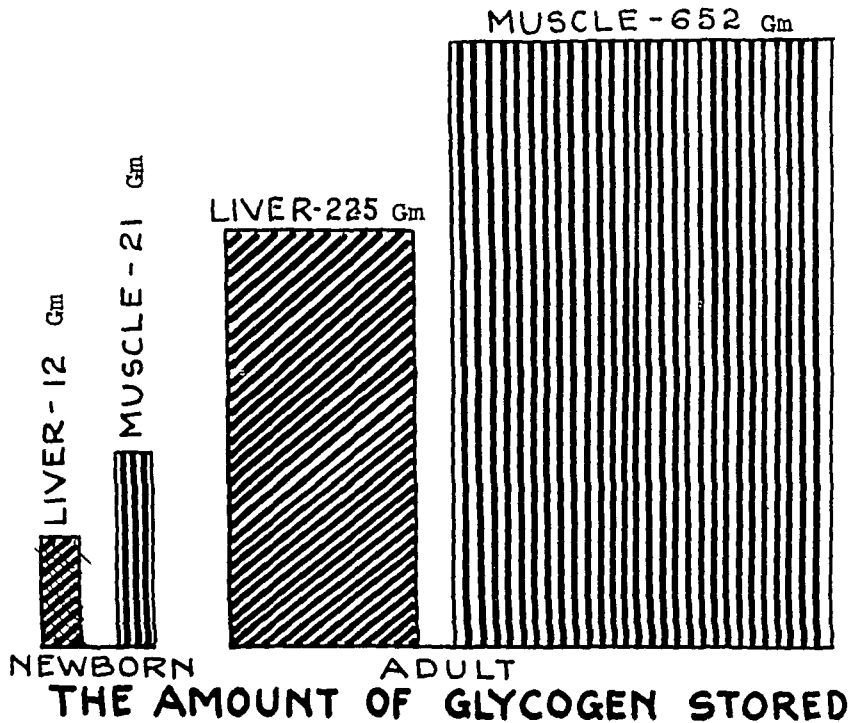


CHART 4—The storage of glycogen in liver and muscles

operation The other 12 surgeons cooperated with me fully and accepted my judgment as to when the patient should be operated upon Table IX shows the results The first six surgeons had no fatalities, and the other six had a comparatively small number of deaths, but the operations performed by the obstinate surgeon resulted in death in 17 per cent of the cases The average mortality rate for the first 12 surgeons is 4.6 per cent, as compared to the 17 per cent of the last operator One can thus readily see how the statistics of one such surgeon can alter unfavorably the record for a whole institution

THE CARE OF SURGICAL DIABETIC PATIENTS—*The Rôle of the Liver* If a clear understanding is to be had of the chemical changes that occur following an operation upon a diabetic patient, attention must be focused on the liver The liver is a storehouse for glycogen which may be drawn upon in time of need This organ does not contain the entire bodily supply of glycogen, for

about two-thirds of it is stored in the muscles (Chart 4) That in the liver, however, represents the portion easily available for use by the body

The liver is concerned in the metabolism of sugar, protein, and fat Its function is to make constantly available, in ample quantity, food for the body in a utilizable form This availability must be independent of the rate of consumption and combustion of ingested food Thus the liver has to store carbohydrates and convert other substances into glucose, when needed, in order to regulate the concentration of sugar in the blood If this function of the liver fails, either hyperglycemia or hypoglycemia is the result The liver also stores protein, and acts on amino-acids to form urea Fat, too, is stored in the liver, sometimes to the extent of 40 per cent of the weight of this organ The quantities of fat and glycogen in the liver bear a reciprocal relation to each other

In addition to these metabolic functions, the liver regulates the formation of bile acids which are important in the absorption of fat and possibly of certain vitamins, its stellate cells remove bacteria from the blood stream, it destroys certain poisons, it regulates the normal process of coagulation of the blood, and it has a part in the maintenance of fluid volume

It is easy to see how important the function of the liver is to a diabetic patient who must have an operation The patient must receive carbohydrate, if the function of the liver is to be supported, and insulin must be taken if the carbohydrates are to be properly utilized The surgeon must bear these facts in mind when he operates upon a diabetic patient, in order to disturb as little as possible the normal function of the liver The type of anesthesia is extremely important in this regard Chloroform may cause severe and possibly fatal hepatic injury, and should never be used in a diabetic patient Ether, by reducing the store of glycogen in the liver, results in hyperglycemia which is directly proportional to the degree of narcosis⁶² (Chart 5) Ether anesthesia also decreases the secretion of bile and depresses the formation of urea and causes an increase in the quantity of fat in the blood If ether anesthesia has to be used in a diabetic patient, these facts must be taken into account, and measures must be instituted to combat them The patient should go to operation with a good supply of glycogen in the liver, and should be protected afterwards from dehydration, hyperglycemia and acidosis ✓

A Special Diagnostic Problem—The diagnosis of conditions which require surgery in the diabetic patient does not offer any special difficulty, except in the case of symptoms of an acute abdominal inflammation In such instances, the differentiation between diabetic acidosis and acute appendicitis must be made The importance of this differentiation is obvious, for to subject a patient with acidosis to an operation needlessly is an extremely hazardous procedure In Table X are summarized the findings in both conditions, and about the only point of difference is that in acute appendicitis the pain precedes the vomiting, whereas in acidosis the vomiting precedes the pain

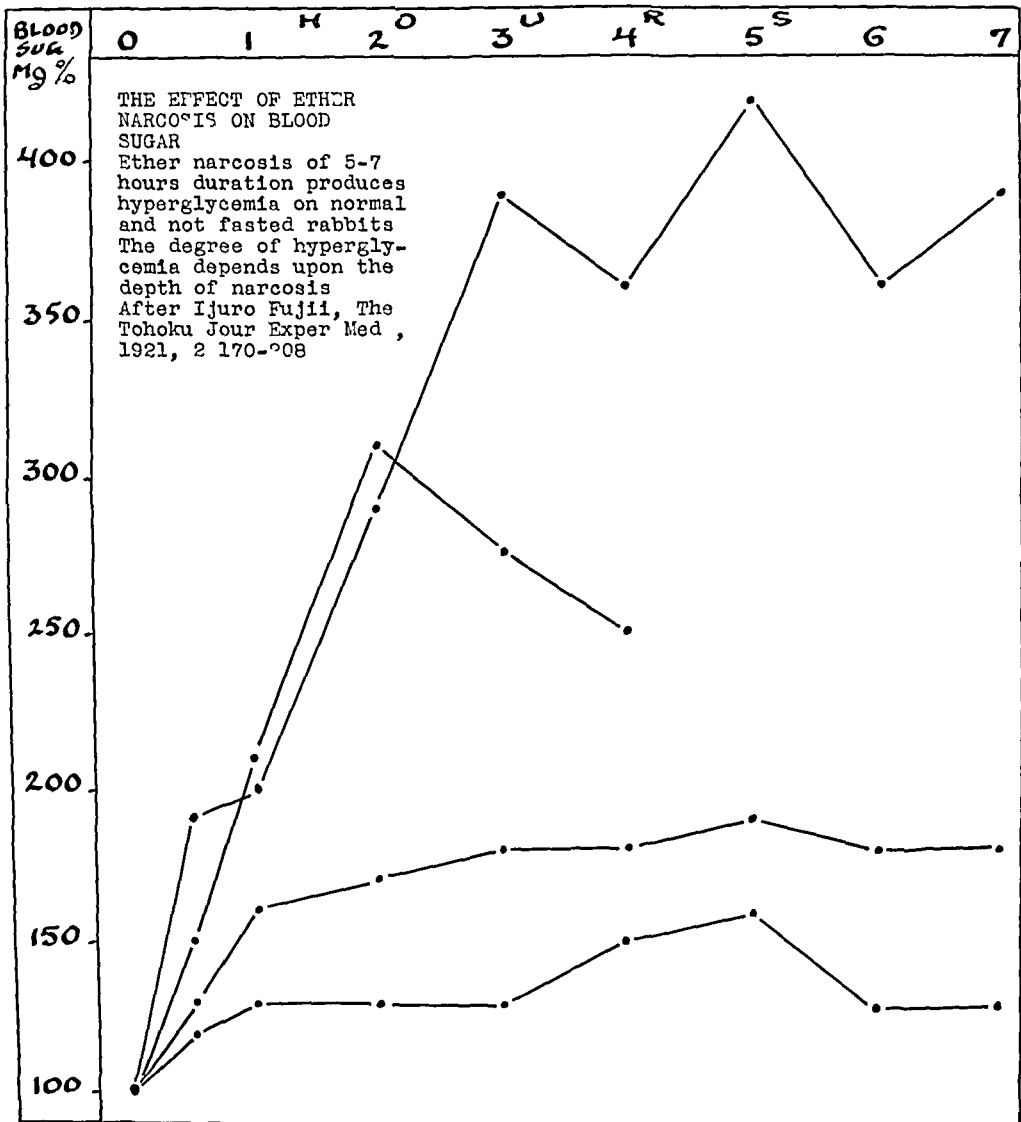


CHART 5—Ordinates Blood sugar Abscissas Hours The effect of ether narcosis on the level of the blood sugar (After experimental studies on rabbits by Ijuro Fujii Tohoku Jour Exper Med, 2 170-208, 1921)

TABLE X

DIFFERENTIATION BETWEEN DIABETIC ACIDOSIS AND ACUTE APPENDICITIS

Symptoms	Acidosis	Appendicitis
Vomiting	Precedes onset of pain	Follows pain
Fever	May or may not be present	May or may not be present
Leukocytosis	Usually high from dehydration and concentration of blood	Usually high and may be significant
Pain	Present	Present

This makes the problem sound quite simple, but such is not the case. In some instances, the patient's notion of the sequence of events is quite hazy, and it is difficult to get an accurate history. Much experience in the handling of diabetic patients usually is necessary before one may have complete assurance in the diagnosis of diabetic acidosis.

The doctor's responsibility, in such instances, is very great, for if operation is not performed in case of acute infection, the patient may have a ruptured appendix and peritonitis, and if operation is performed in an instance of acidosis, the patient is quite likely not to survive the shock. The best thing to do, in my opinion, is to give intravenously 500 cc. of a 10 per cent solution of glucose containing 20 to 40 units of insulin. If, within an hour or two, the symptoms are not relieved, they are most probably due to appendicitis, and the patient should be operated upon. It is usually safe to defer the operation for an hour, and this wait may be responsible for saving the patient's life.

The Preparation of the Patient for Surgery—We have already seen that, if surgical results are to be good, and the risk of operation decreased in diabetic patients, the metabolic disorder must be taken into account every step of the way, and must be controlled as rigidly as possible if disaster is to be avoided.

In the preparation of diabetic patients for operation, the measures used have to be adjusted to the emergency or urgency of the situation. In case of an emergency operation, there naturally is no time for any deliberative or systematic study of the patient's condition. Even so, usually 30 to 60 minutes elapse from the time the patient enters the hospital until he appears on the operating table. This affords ample time for a urine analysis and an estimation of the blood sugar, which requires but 25 to 30 minutes. If the level of the blood sugar is high, the patient receives 20 units of insulin before the operation is begun.

When there is no immediate hurry about the operation, a thorough study of the patient can be made. It is possible to get the diabetic condition under control and to determine the patient's individual sensitivity to insulin. The diabetes is considered well controlled when the 24-hour sugar output is below 10 Gm. The variations in utilization of insulin are determined by the level of the blood sugar before breakfast, lunch and dinner. These indicate how the insulin dosage should be distributed throughout the day. Patients are no longer starved before an operation. They usually receive from 160 to 200 Gm. of carbohydrate, 70 to 100 Gm. of protein, and enough fat to make 1,800 to 2,200 calories, according to the individual needs. In patients with gallbladder disease, the fat naturally is kept to a minimum. The study made by the internist is directed toward finding out just what the dosage and distribution of insulin should be to enable the patient to utilize such a diet.

One blood sugar determination is practically worthless as a guide to a diabetic patient's condition. The blood sugar often fluctuates so much during the day that a single determination may be very misleading. It is not neces-

sary that operation be deferred until all three daily levels of blood sugar are exactly normal. If the patient's urine is sugar-free, and the level of the blood sugar below 200 mg per cent, the operation can be performed with safety, provided the proper control is maintained. The important thing is to know just how much insulin the patient needs.

The morning of the operation, the patient receives his regular morning dose of insulin, a glass of orange juice, and a cup of coffee, at least two hours before the operation is to be performed. This helps to stock the liver with glycogen, and the patient does not feel so worn-out and hungry.

Protamine insulin can be used in surgical cases, although I prefer to use regular insulin during the preoperative and immediate postoperative periods. There is greater safety with small, frequent doses of insulin, than with one large dose of protamine insulin. The latter can be resumed during convalescence, when all emergency has passed.

TABLE XI
EFFECTS OF ANESTHESIA

Type	Effect
Local—procain	Least effect on insulin activity
Barbital derivatives—sodium epival	Least reduction of liver glycogen
Spinal—procain	Reduction of glycogen in voluntary muscle and heart
Gas—nitrous oxide, ethylene, cyclopropane	Increase of lactic acid inhibits formation of glycogen in muscle
Ether	Production of lactic and phosphoric acids in muscle augments acidosis

Anesthesia—The importance of the choice of anesthetic for a diabetic person has already been mentioned, in connection with its effect on hepatic function. Chloroform, because of its hazardous effects, has not been used in this country for about 30 years. Ether has many disadvantages, although with the proper precautions it can be used satisfactorily. This anesthetic is used largely at the Mayo Clinic, where surgical results are so excellent. If local or spinal anesthesia can not be employed, nitrous oxide, ethylene, and cyclopropane are the anesthetics of choice. The effects of these various anesthetic agents are summarized in Table XI. In general, the deeper the narcosis produced by an anesthetic, the greater the inhibition of oxidation of glucose and lactic acid in the brain. Chart 6 shows the increase in blood sugar in a series of diabetic patients as determined by studies immediately before and after operation. The greatest increase occurred in patients who were anesthetized with ether.

Postoperative Care—In the case of the diabetic patient who has been subjected to an emergency operation, the study must be continued immediately following operation. Just after he has returned from the operating

SURGERY AND DIABETES

100m, another blood sugar estimation is made. At the same time 20 units of insulin are administered, with hypodermoclysis of a normal solution of sodium chloride and 5 per cent glucose. If indicated by the patient's condition, 500 cc of a 10 per cent solution of glucose may be given intravenously. The level of the blood sugar is determined at two-hour intervals for the next six to eight hours, and then three times a day for the next two days. This keeps the physician informed regarding the patient's condition, and

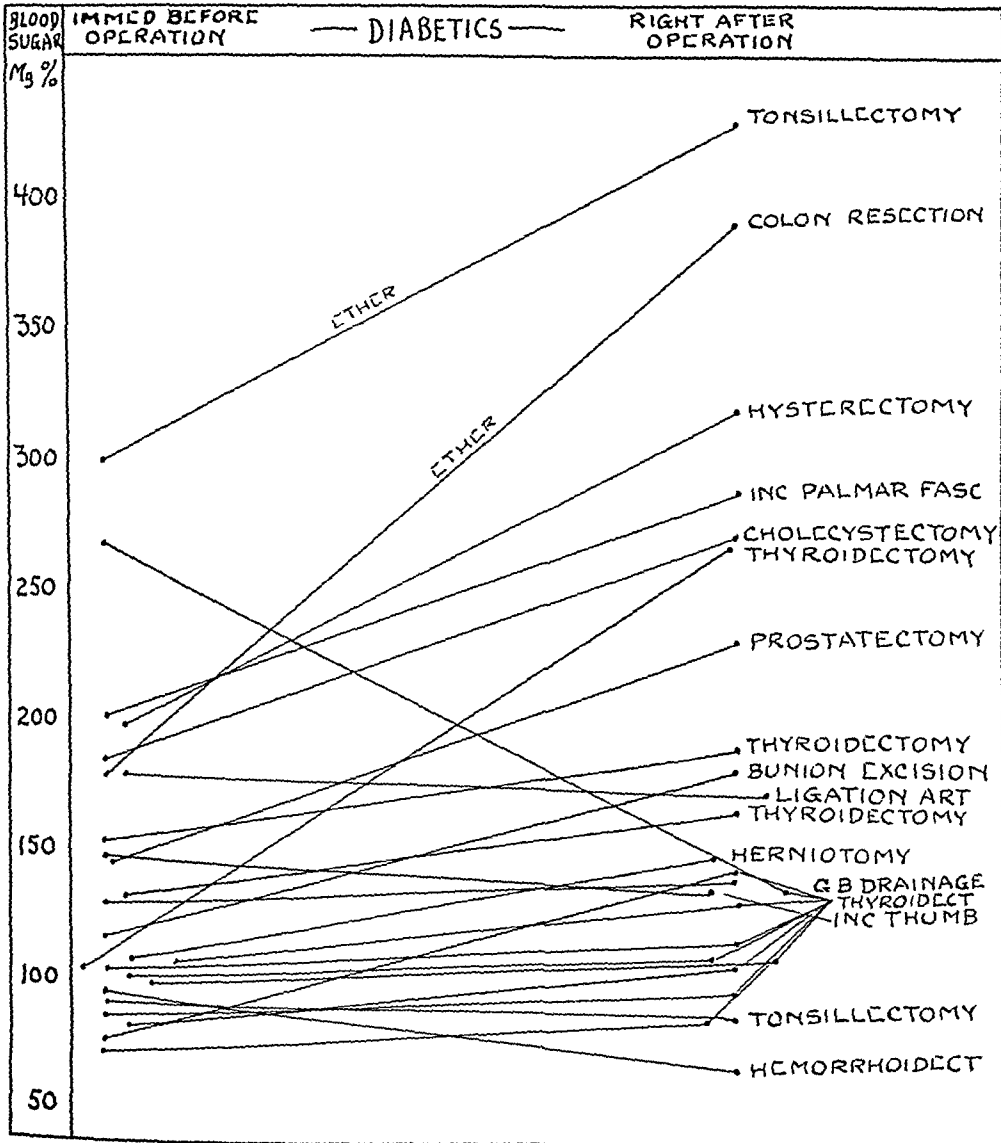


CHART 6—Ordinates Blood sugar Abscissas Effect pre and postoperative The effect of anesthesia on the level of blood sugar

averts serious fluctuations in the blood sugar level. If it is impossible to check the blood sugar in this way, urine estimations must be made frequently, but the sugar in the blood is an infinitely better guide to the patient's condition. It must be remembered that acidosis is much more serious than large quantities of sugar in the urine.

The treatment in cases studied adequately before operation is much the same afterwards as that of the emergency cases. The administration of salt solution and glucose by hypodermoclysis or by vein, and sufficient insulin to

keep the blood sugar under control, with repeated checks of the blood are carried out. Within 24 to 48 hours, the emergency has usually passed, and the patient can safely be returned to his usual regimen.

POSTOPERATIVE COMPLICATIONS—*Intravenous Injection of Glucose*—The use of glucose and salt solutions is a common procedure in caring for non-diabetic patients after operation, both in preventing and combating postoperative complications. It has been found that the same measure can be employed in diabetic patients provided sufficient insulin is given to allow the patient to utilize the glucose. This has been recommended by numerous authorities, including Thalheimer,⁶³ Fisher^{64, 65, 66} Ringer,⁶⁷ Ginsberg,⁶⁸ and Levy.⁶⁹ Before the advent of insulin, this protective measure could not be used in diabetic patients, for any addition of glucose to the already increased quantity of sugar in the blood would have been dangerous. But now, if the proper quantity of insulin is added to the glucose-saline solution, the diabetic patient is protected from excessive hyperglycemia.⁷² Table XII shows a summary of the fluctuations in blood sugar following intravenous injections of glucose solution in 54 patients with diabetes, who either had had an operation, or were suffering from diabetic acidosis. In the latter condition, the intravenous injection of glucose and insulin is especially valuable in combating the acidosis and increasing the excretion of ketones in the urine, and in augmenting the supply of glycogen in the liver. About two or three hours after glucose solution has been given, the patient's blood sugar should be checked, when more insulin can be supplied, if needed.

Glucose solutions are indicated in the following postoperative conditions (1) After an operation of long duration, (2) when a large quantity of anesthetic has been used, (3) as a temporary measure before transfusion after profuse loss of blood, (4) in the event of possibility of severe surgical shock, (5) whenever there is the slightest danger of postoperative peritonitis.

Blood Transfusions—Blood transfusion is perhaps the most helpful single measure available for combating postoperative complications. Transfusions are indicated in the following instances (1) After profuse hemorrhage with reduction of blood volume, (2) in the presence of infections, and (3) in all cases which present a poor surgical risk, either because of the condition of the patient, or the extensive nature of the operation.

In administering a transfusion to a diabetic patient, it is well to remember, as Staub⁷⁰ has pointed out, that the blood of the donor has an action resembling that of insulin if he has eaten a heavy carbohydrate meal from four to seven hours previously.

Fever—An increase in temperature always means increased metabolism. The fever in a diabetic patient may be the result either of toxemia or infection, and it is important to differentiate these two conditions.

When fever is present before an operation, a blood culture should be made. If the culture is positive, the patient, of course, should not be operated upon immediately but an attempt should be made to rid him first of the septicemia. If fever continues after the operation in a patient whose blood

culture was negative before, the culture should be repeated three days after the operation

TABLE XII
CHANGES IN BLOOD SUGAR LEVELS AFTER INTRAVENOUS INJECTION OF GLUCOSE IN FIFTY-FOUR CASES

Case	Fall	Rise	Case	Fall	Rise
	Mg per Hour			Mg per Hour	
1	22	—	28	—	22
2	24	—	29	—	14
3	60	—	30	28	—
4	33	—	31	25	—
5	19	—	32	11	—
6	38	—	33	10	—
7	28	—	34	8	—
8	34	—	35	14	—
9	10	—	36	208	—
10	26	—	37	6	—
11	47	—	38	3	—
12	—	38	39	—	5
13	—	18	40	4	—
14	39	—	41	4	—
15	58	—	42	9	—
16	24	—	43	18	—
17	18	—	44	22	—
18	—	—	45	—	0 3
19	—	—	46	38	—
20	28	—	47	50	—
21	34	—	48	24	—
22	10	—	49	16	—
23	26	—	50	22	—
24	47	—	51	28	—
25	—	38	52	61	—
26	—	20	53	33	—
27	1 8	—	54	19	—

Fall—44 cases (81 5%)—Average 29 3 mg
Rise— 8 cases (14 8%)—Average 19 3 mg
No change—2 cases (3 7%)

In the toxemia resulting from infection, the patient often suffers from anorexia, and hence the intake of food is diminished Nausea and vomiting may make it impossible for the patient to take any food or liquids In such instances, with increased metabolism from the fever and little or no food supply, protein and fat catabolism are increased This means production of urea nitrogen from the protein and of ketone bodies from the fat The already impaired glycogen reserve of a diabetic patient is depleted after several days of fever, so that there is insufficient carbohydrate to aid in the complete

oxidation of the fat. Hence it is imperative that more carbohydrate be supplied, which is accomplished by the intravenous injection of glucose and sodium chloride solutions, in conjunction with the proper quantity of insulin.

Unconsciousness—When a diabetic patient becomes unconscious after operation, it is important to differentiate between surgical shock, diabetic coma, hypoglycemia and alkalosis. In this differentiation, the history is of extreme importance, as well as the blood chemical determinations. Once the diagnosis has been made, the remedy is obvious (Table XIII).

TABLE XIII

DIFFERENTIATION OF POSTOPERATIVE COMPLICATIONS IN A DIABETIC PATIENT

Findings	Surgical Shock	Diabetic Coma	Hypoglycemia	Alkalosis
Unconsciousness	Present	Present	Present	Present
Temperature	Low	Subnormal		
Pulse rate	High			
Respiration	Increased	Kussmaul Acetone breath	Normal	
Urine analysis		Sugar and acetone present		
Blood chemistry		Sugar high, CO ₂ usually below 20	Sugar low	
Perspiration			Profuse	
Dehydration		Present		
Convulsions				Present
Tetany		.		Present
History	Injury or operation	Infection or lapse of diet	Insulin injection	Alkalies in large quantity
Miscellaneous	Capillary distention, dilatation of splanchnic vessels, toxemia	Soft eyeballs, low spinal pressure	Strabismus at times	

The patient suffering from surgical shock should receive glucose and insulin intravenously, and external heat should be applied.

For the treatment of diabetic coma, large doses of insulin, saline solution by hypodermoclysis, glucose solution by vein, external heat and gastric lavage and enemata are used. In the presence of acidosis, gastric lavage is an extremely important measure. In one instance in my experience, the patient died because of failure to carry out this measure. It was one of those

cases in which the differentiation of acidosis and appendicitis was vital. The patient was suffering from acidosis which was brought under control by the use of insulin, glucose and salt, but the patient died. The autopsy showed that he did not die from cardiac failure, but from respiratory failure due to regurgitation of gastric contents into the trachea, and consequent filling of the lungs. Since this experience, I have never failed to stress the fact that gastric lavage is essential in the treatment of diabetic acidosis.

When a patient is suffering from insulin shock or hypoglycemia, a 50 per cent solution of glucose should be given intravenously.

In the case of alkalosis, sodium chloride solution either intravenously or by hypodermoclysis should be given.

Renal Insufficiency—The accumulation of waste products in the blood, as shown by high levels of urea, uric acid, and creatinin may result from anhydremia as well as from actual renal damage, in a diabetic patient. Unless there is considerable edema, infusions of sodium chloride solution (2 to 3 liters) containing glucose, or along with glucose solution administered intravenously, present the best method of treatment. At times, salt solutions containing 5 per cent glucose may be given by proctoclysis. Unless there is severe renal damage, administration of fluids tends to reestablish the normal status.

The use of Fischer's solution is helpful when there is marked depression of renal function. In 1931, I⁷¹ reported the case of a man, age 26, who had acidosis and extreme oliguria. The kidney function was almost completely absent, as shown by no excretion following injection of phenolphthalein, and high levels of urea, uric acid and creatinin. This condition continued for five days, despite large doses of insulin (200 units a day). On the fifth day I gave him 500 cc of Fisher's solution intravenously, and the urine output increased to more than six liters, after having been only a few hundred cubic centimeters daily. The urea, uric acid, and creatinin returned to normal levels, and the kidney function, as determined by the phenolsulphonphthalein test, was 70 per cent in two hours. From this and other experiences, I feel that Fisher's solution has a place in the treatment of cases of this type.

Anoxemia—Anoxemia is a rather common surgical complication, especially in cases in which prolonged anesthesia has been required. The clinical signs of this condition include excitability, stimulation, headache, rapid pulse and a dusky appearance of the nails. These symptoms appear before the patient becomes frankly cyanotic. Increasing the patient's supply of oxygen by means of the oxygen tent is the treatment for this condition. The oxygen tent should be applied before the patient becomes actually cyanotic, and the reasons for its use should be explained to him, in order to secure his cooperation. A supply of four to five liters of oxygen each minute is usually administered, although higher concentrations which furnish as much as 15 liters per minute may be used.

It is well to use the oxygen tent as a prophylactic measure in patients who have had prolonged general anesthesia. The patient should receive inhalations of 5 per cent carbon dioxide with 95 per cent oxygen, for 15 to 20 min-

utes three times a day for three or more days after operation. This measure aids expansion of the lungs, insures a better aerating surface, and prevents atelectasis, and hence is prophylaxis against postoperative pneumonia.

SUMMARY AND CONCLUSIONS

Since the use of insulin in the care of diabetic patients, the surgical mortality rates in this type of case have decreased tremendously. An average of a series of 1,767 cases reported before the advent of insulin showed a mortality rate of 20.6 per cent, while in 9,513 cases reported since 1923, the mortality has been only 6.7 per cent. There are still tremendous variations in the results reported. These range from 1.2 to 68 per cent.

Surgery in diabetic patients carries a greater than normal risk, not because of the diabetes *per se*, but because of obesity, arteriosclerosis, advanced age, and the dangers of infection.

Cholecystitis is common among diabetic patients, and the removal of the gallbladder usually improves the diabetic condition.

Surgery of the extremities for gangrene is a special problem encountered in diabetes. The best treatment for gangrene is prevention, because the mortality rates in this type of operation are necessarily high, owing to the advanced age of the patients and the shock occasioned by amputation.

The proper care of a diabetic patient who has an operation demands the combined services of an internist and surgeon who are interested in the disease. The best results are obtained where there is the best team work.

A proper understanding of the function of the liver is necessary to provide the proper precautions for the diabetic patient who undergoes operation.

The most important diagnostic problems encountered in connection with surgery on diabetic patients are (1) The differentiation between acute appendicitis and diabetic acidosis, and (2) the proper diagnosis of unconsciousness which may appear following an operation. The latter may be caused by surgical shock, diabetic coma, hypoglycemia or alkalosis. The history and blood chemistry findings are important in making this differentiation.

Except in situations that present an emergency, a diabetic patient should be subjected to thorough study before any surgical procedure is attempted. The proper dosage and distribution of insulin must be determined, if the diabetic condition is to be kept under control satisfactorily after the operation.

The choice of anesthesia is very important. Chloroform should never be used, ether has a great many hazards. The anesthetics of choice, when local or spinal anesthesia can not be used, are nitrous oxide, ethylene, and cyclopropane.

After an operation, the condition of the diabetic patient must be followed most carefully, with repeated determinations of the blood sugar, and adjustment of the insulin dosage, so as to prevent both hyperglycemia and hypoglycemia. Glucose intravenous solutions can be used, provided they are accompanied by appropriate doses of insulin.

Blood transfusions are of great help in preventing and combating post-operative complications

Fever and anorexia bring about metabolic changes, with dehydration, accumulation of waste products, and hyperglycemia, which can be corrected only by the use of intravenous solutions of salt and glucose and insulin

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STRANGULATED LITTRÉ'S FEMORAL HERNIA WITH SPONTANEOUS FECAL FISTULA

CASE REPORT WITH A REVIEW OF THE LITERATURE

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ALEXIS LITTRÉ,¹ in 1700, described three cases of hernia in which an intestinal diverticulum alone was strangulated. It was his belief that the diverticula were the result of traction on a portion of bowel in the hernia, a condition now associated with the name of Richter.² There is no proof that this was not the case.

Johann Meckel,³ in 1810, over 100 years later, first classified the different types of intestinal diverticula. His name is now associated specifically with that diverticulum which is derived from an incompletely obliterated vitelline duct.

According to Thompson,⁴ Meckel's diverticula in the vast majority of cases are found within the terminal four feet of the ileum, their size varies greatly, the average being about one inch in length with a fairly broad base. He groups the anatomic types most commonly seen as

"1 The typical diverticulum given off from the antimesenteric side of the ileum, lying free in the peritoneal cavity, and presenting a closed distal extremity (82.5 per cent)

"2 Partial obliteration with a fibrous band running from the tip of the diverticulum to the umbilicus or to some adjacent structure (10 per cent)

"3 Umbilical fistula (6 per cent)

"4 The giant diverticulum of bizarre form or shape, sometimes coming off from the mesenteric side of the ileum and developing between the folds of the mesentery (0.5 per cent)

"5 The umbilical polyp, either attached to the remains of the omphalomesenteric duct inside the abdomen, or entirely cut off from intestinal connections (0.5 per cent)

"6 The simple intramesenteric variety (0.5 per cent)"

Obviously from the standpoint of both occurrence and anatomy, the diverticulum falling into Thompson's first group is the only one likely to be found in an inguinal or a femoral hernia. The intramesenteric diverticulum of large dimensions in group 4 has, by many, been considered a reduplication of the ileum.

It is through common usage that the title of Littré's hernia is applied only if the diverticulum is of Meckel's type, and is the sole occupant of the hernial sac.

Mason⁵ notes the postulates expressed by Littré, who ascribed his difficulty in diagnosing his cases to the fact that the constricting force, falling on the pedicle of the diverticulum, did not interrupt the continuity of the lumen of the gut. The following are Littré's own rules as transcribed by Mason:

"The diagnostic signs, making this type of hernia recognizable before the operation, are

"1 The patient goes to stool during the whole course of the illness as, the intestinal canal being uninterrupted, the excrements are at perfect liberty to pass from one end to the other

"2 The patient has no hiccough, or very occasionally

"3 He does not vomit, at least by comparison less frequently than in ordinary herniae. The vomitus is never fecal matter

"4 The patient's belly is never fat, stretched or full of wind as in ordinary herniae

"5 The tumor in the groin is formed more slowly and never becomes so large

"6 The inflammation, fever, pain or other symptoms which may accompany this peculiar kind of hernia, are less severe and take longer to manifest themselves than in other herniae

"The diagnostic signs which make this particular hernia recognizable during the operation are

"1 In ordinary cases of hernia, the entire circumference of the intestinal body is engaged in the hernial sac. In this hernia there is only one part in the sac

"2 The portion of the intestine which forms an ordinary hernia is found doubled in the shape of an arc in the sac. In this particular kind (which concerns us), this portion is single, situated perpendicularly and terminated by a very distinct end

"3 An ordinary hernia is often formed by intestine and omentum together. This particular kind is always made by the intestine alone."

Such instructions, although formulated over two centuries ago, require today little, if any, correction or amplification.

Friedman⁶ states that death is the inevitable fate of the patient with a strangulated hernia, unless the resulting obstruction is relieved by operative interference, spontaneous reduction of the hernia or the formation of an external fecal fistula. He further states: "The pathologic changes taking place in the formation of a fecal fistula are in the beginning like those of any strangulated hernia: first, there is an exudation of a bloody fluid into the hernial sac, and with impairment of integrity of the bowel, infection of the fluid. As the sac wall becomes infected and edematous, the bowel perforates into, and then through the sac, thereby involving the external hernial coverings. Infection and necrosis then spread rapidly through the subcutaneous tissues, and finally rupture occurs externally through the skin, forming an external fecal fistula."

Watson⁷ states that in Littlé's, as in appendiceal hernia, inflammation is

much more frequent than strangulation, when so-called "strangulation" occurs it is nearly always secondary to the inflammation and infection. True strangulation of a Meckel's diverticulum is rare. Sometimes it is impossible to determine whether inflammation or strangulation occurred first. With reference to location he says "Strangulation of the isolated hernia of Meckel's diverticulum is more frequent in femoral than in inguinal hernia."

Appended is a report of a case of spontaneous fecal fistula resulting from a strangulated Littre's femoral hernia, which was observed and operated upon at the Vanderbilt University Hospital.

Case Report—A S, an unmarried white female, age 49, first came under the observation of the Medical Service March 30, 1935. She was treated for idiopathic migraine. Routine examination disclosed no suggestion of hernia. On November 29, 1935, when next seen, she gave a history of having had, four days previously, colicky pains in the lower midabdomen, followed shortly by the appearance of a swelling in the right groin. There was no nausea, emesis or obstipation.

Physical Examination disclosed a hard mass in the right groin over which the skin was reddened and slightly warmer than the surrounding region. There were no other enlargements in the glandular areas or open lesions on the lower extremities. Rectal and pelvic examinations revealed nothing abnormal. Leukocytes, 6,550. The impression conveyed at this time was that of an inguinal adenitis of unknown origin, and the patient was sent home to bed and instructed to use alternating hot and cold packs to the groin. On December 13, 1935, two weeks later, the only noticeable change was a decrease in redness of the skin.

On December 27, 1935, examination revealed a draining sinus at the site of the mass in the right groin, which the patient said had occurred nine days previously. She was referred to the Surgical Out-Patient Service where a hernia was suspected and, with the history of a large amount of green drainage increasing with ingestion of food, fecal fistula was diagnosed.

On January 2, 1936, the patient was admitted to the Surgical Ward where additional questioning revealed that six weeks ago, after going two days without a stool, she was seized with colicky pains which lasted 24 hours, but were not accompanied by nausea or vomiting. She took salts and had a stool the same night and the next morning. During the day of colic, the mass in the right groin had appeared and become as large as a lemon and gurgling was noticed in this region.

Physical Examination revealed a white female rather thin and drawn but not dehydrated. The abdomen was neither tender nor distended. There was borborygmus audible, but no visible peristalsis. In the right groin there was a small reddened, slightly tender, fluctuant mass about 6 cm in diameter lying immediately over the inguinal ligament. In the center of this mass there was a peaked crater from which thin greenish material and a few small bubbles were expressed. On vaginal examination, the introitus admitted only one finger. There was a fulness in the right fornix, pressure upon which did not increase the flow from the sinus in the groin. Temperature was 99.6° F. Leukocytes, 5,600. Tests for bile and tubercle bacilli in the sinus drainage were negative. Carmine taken by mouth failed to pass in recognizable quantities from the sinus, a biopsy from which showed only granulation tissue. *Impression* at this time was Fecal fistula resulting from perforation of a strangulated Richter's hernia in the right femoral region.

On the fifth day after admission, with the idea that closure might occur spontaneously, the patient was discharged and told to report to the Surgical Out-Patient Service. *Roentgenologic Examination* of the gastro-intestinal tract showed "Esophagus, stomach and duodenum are normal. On the five-hour examination, the terminal ileum is shown filled and lying beneath the sinus. At six and twenty-four hours no portion of the large

bowel could be demonstrated communicating with the draining sinus. The cecum and appendix lie some distance away from the sinus. An irregular calcification overlying the right wing of the sacrum was seen. Fluoroscopic examination of the dressing over the sinus shows a radiopaque material, probably barium."

Operation—January 22, 1937, by Dr. Barney Brooks. "An incision to the right of the midline below the umbilicus was made. On entering the abdominal cavity, a characteristic Meckel's diverticulum, the tip of which was buried in the right femoral canal, was found. Attempt was made to dislocate the tip of the diverticulum from the femoral canal from within the peritoneal cavity. It was obvious, however, that this could not be safely done. Incision was, therefore, made parallel to Poupart's ligament through the fistulous opening, dividing the ligament over the femoral canal. This permitted freeing the tip of the diverticulum which was then resected, the wound in the ileum being closed with inverting continuous catgut sutures. A very irregular partially calcified cystic tumor of the right ovary, densely adherent to the wall of the pelvis, was extirpated. The abdomen was closed with continuous catgut for the peritoneum, interrupted silk for the fascia, subcutaneous tissues and skin. The inguinal ligament was resutured and the incision over it was loosely closed. A small rubber tissue drain was left in this wound. Because of the existing infection, no attempt was made to repair the hernia at this time."

Pathologic Examination showed the diverticulum to be 4 cm long and 3 cm wide at the base. There was a perforation at the tip. There was no evidence of gangrene at the time of operation. No gastric mucosa was found in the diverticulum.

The patient's recovery was uneventful and she was discharged on the fifteenth post-operative day. The inguinal wound was entirely healed one week later.

On April 8, 1937, the patient was readmitted for a repair of a right femoral hernia which was easily reducible but the source of some discomfort. A radical repair was accomplished by Dr. Barney Brooks. Convalescence was uneventful. The patient has been followed in the Out-Patient Service and has, apparently, remained cured.

Discussion—Of 1,334 strangulated inguinal and femoral herniae, collected by Frackau,⁸ 654 were inguinal, of which 89 per cent occurred in males and 11 per cent in females, 680 were femoral, of which 21 per cent were in males and 79 per cent in females. Between September 15, 1925, and June 1, 1937, 16 cases of strangulated femoral hernia were observed in Vanderbilt University Hospital. Of these, seven were in males and nine in females.

In a series of 21,693 autopsies compiled by Pabst,⁹ Meckel's diverticulum was found 285 times, or in 0.9 per cent of the postmortem examinations. Christopher¹⁰ states that 0.8 per cent of 1,382 patients coming to autopsy at the Boston City Hospital as well as of 2,000 at the Johns Hopkins Hospital were found to have a Meckel's diverticulum. In 1,511 autopsies performed in the Vanderbilt University Hospital during the period 1928-1936 inclusive, a Meckel's diverticulum was found six times, or in 0.4 per cent.

According to Christopher, in 10,000 celiotomies studied by Balfour, a Meckel's diverticulum was found in 15 patients, an occurrence of 0.14 per cent. In approximately 3,600 celiotomies at the Vanderbilt University Hospital, a Meckel's diverticulum was found in eight patients, an incidence of 0.22 per cent.

In 600 cases of Meckel's diverticulum, collected by Foigue and Riche,¹¹ only 52, or 8.7 per cent, of the diverticula were found in herniae. In analyzing this collection of 680 cases of strangulated femoral herniae, Frackau⁸ notes that a Meckel's diverticulum was found in only one hernia.

In a review of the literature, there were 32 instances in which a Meckel's diverticulum was found in a strangulated or incarcerated femoral hernia. The present case report brings the total to 33. The designations strangulated and incarcerated were not always in keeping with the description of the operative findings, so that, in the light of accepted definition, liberty has been taken to interpret them correctly. As a result of this correction, 24 of the 33 cases are accepted to be strangulated femoral herniae of Meckel's diverticulum. Table I shows the analysis of the data referable to these 24 cases.

TABLE I

ANALYSIS OF COLLECTED CASES OF FEMORAL HERNIA CONTAINING STRANGULATED
MECKEL'S DIVERTICULA*

Case No	Original Author	Date	Sex	Age	Vomit- ing	Obsti- pation	Perforated	Result
1	Hager	1884	F	55	No	No	No	Recovered
2	Tilling	1701	F	—	—	—	No	Died
3	Martin	1765	M	40	Yes	Yes	Through skin	Died
4	Escher	1891	—	35	—	—	Through skin	Recovered
5	Minter	1835	F	44	—	—	Into sac	Died
6	Busch	1884	M	53	—	—	Into sac	Died
7	Riecke	1834	F	50	Yes	Yes	No	Died
8	Ekehorn	1901	M	38	No	No	No	Recovered
9	Taignon	1700	F	60	—	No	Through skin	Recovered
10	Hasenhorhl	1773	F	38	Yes	Yes	No	Died
11	Raesfeldt	1852	F	30	Yes	Yes	No	Died
12	Howse	1874	M	37	—	—	No	Died
13	Hofmohl	1885	F	76	—	—	Through skin	Recovered
14	Dutil	1886	F	56	Yes	No	Into sac	Died
15	Mugnai	1898	F	40	—	—	No	—
16	Smith	1901	F	34	Yes	No	No	Recovered
17	Hilgenreiner	1903	F	74	No	No	Through skin	Recovered
18	Riviere	1907	M	44	No	No	No	—
19	Harrington	1926	F	55	—	—	No	Recovered
20	Sweet	1930	M	72	No	No	No	Recovered
21	Sinclair	1922	F	55	No	No	Into sac	Recovered
22	Donati	1931	M	79	—	—	No	Recovered
23	Mason	1933	F	—	No	No	No	Recovered
24	Author	1937	F	49	No	No	Through skin	Recovered

* Strangulated by definition

Cases 1 through 8 collected by Ekehorn¹²

Cases 9 through 18 collected by Pabst⁹

Cases 19 and 20 collected by Sweet¹³

Cases 21 through 24 collected by author

The author has been able to find records of only 23 cases of strangulated femoral hernia of Meckel's diverticulum in the literature from 1700 to the present time. Of these, seven, or 29 per cent, were in males, and 16, or 67 per cent, were in females. In one the sex was not recorded. The youngest patient was 30 and the oldest 79 years of age. In two cases the age was not noted. The age distribution showed six in the fourth decade, five in the fifth

decade, six in the sixth decade, one in the seventh and four in the eighth decade. The average age was 50 years.

Of the 14 cases in which information was available, six, or 43 per cent, had vomiting. Of the 15 cases in which obstipation was noted, it occurred only four times, or in 27 per cent.

Six cases perforated through the skin, forming external fecal fistulae. Of these only one, or 16.6 per cent, died. Of the four that perforated into but not through the sac, three, or 75 per cent, died.

All might be designated Littre's herniae except Case 12, which contained strangulated omentum in addition to the strangulated diverticulum, and Case 21, whose sac contained both a Richter's hernia of the ileum and a perforated Meckel's diverticulum. In Cases 3 and 4, ascariis worms were observed coming from the fistulous openings. In Case 4, the fistula healed spontaneously and the Meckel's diverticulum was discovered later when the persistent hernia was operated upon.

In analyzing the six cases in which a fecal fistula occurred spontaneously, it was found that one was in a male, four in females, and one in which the sex was not recorded. The ages of the patients were 35, 40, 49, 60, 74 and 76, the average being 56.

In one there was vomiting and in two cases there was no vomiting. No mention was made of this symptom in the other three cases. Obstipation was present in one patient, in three it was absent, and in the remaining two, no information was available. The patient who died was a male, age 40, who had both obstipation and vomiting. This patient was the only one, of this series of six, with spontaneous fecal fistula from strangulated Littré's femoral hernia, to have either obstipation or vomiting.

SUMMARY

- (1) Littré's hernia has been defined.
- (2) The symptoms and signs of Littré's hernia, as transcribed by Mason, are noted.
- (3) A case of spontaneous fecal fistula from a strangulated Littre's femoral hernia is reported.
- (4) A Meckel's diverticulum was found in 0.9 per cent of 21,693 autopsies, while in two groups of 1,382 and 2,000 postmortem examinations, the same structure was found in 0.8 per cent of the cases. In the Vanderbilt University Hospital, in six, or 0.4 per cent, of 1,511 autopsies a diverticulum was found.
- (5) A review of the literature, from 1700 to the present time, revealed that, including the present case, 24 instances of strangulated hernia of a Meckel's diverticulum were reported.
- (6) In six of the 24 cases of strangulated hernia of a Meckel's diverticulum, there occurred a spontaneous fecal fistula. In this group, only one patient died. In four instances in which there was a perforation into but not through the sac, three of the patients died.

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THE PERINEAL TESTIS

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INCIDENCE—In 1786, John Hunter⁶ described two cases of perineal testes. Culling gave the first detailed description of the condition, in 1841, and collected nine cases. In 1879, Annandale reported the first successful operative cure.

Weinberger,¹⁴ in 1879, compiled 74 cases of perineal ectopy. Muschat,¹⁰ in 1933, collected 23 more reports and added one of his own. Campbell, in 1936, stated that 99 cases have been recorded in the available literature and reported three personal cases. The fact that only slightly more than 100 cases of perineal testes have been recorded in the literature indicates the comparative rarity of the condition.

It is generally accepted that the incidence of an undescended testis is once in every 500 men. Godard found three perineal testes in 53 cases of imperfect descent. Burdick and Coley¹ did not encounter a perineal testis in 537 instances of cryptorchidism. Campbell² did not observe one instance in the records of 18,000 autopsies of males. He also states that there was not a single case recorded in 36,000 admissions to the Urologic Service of Bellevue Hospital, New York City. Eccles found five perineal testes in 936 instances of imperfect descent. Over a 17 year period, there occurred 15 cases among 737 imperfectly descended testes seen at the Hospital for the Ruptured and Crippled at Boston (Coley³). While rare, the perineal testis is more common than the pubopelvic or femoral ectopies (McGregor⁹).

Etiology—McGregor accounts for this failure of descent of a testis on an anatomic basis. He found that "In the perineal region there exist on each side two ridges of fascia which separate three pouches. The perineoscrotal reduplication of Colles' fascia separates the scrotal from the superficial perineal pouch. This reduplication forms a smooth ridge. The fascia of Colles here doubles back on itself at an acute angle in the adult dependent scrotum and at a right-angle in the fetal scrotum. The testis or gubernaculum, having traversed what he calls the third inguinal ring, passes down the scrotal neck and arrives at this ridge. At the sixth month, there is a well marked scrotal pouch in the vast majority of cases. Should the fascial reduplication narrow or occlude the orifice, the testis cannot enter the scrotum and may pass posterior to it into the perineum."

Heredity has been considered a factor in the etiology, Godard mentioned a case where father and son both had a perineal testis.

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Sonneland¹³ believes that many perineal testes are traumatic rather than congenital in origin. That a scrotal or inguinal testis may be luxated to a perineal position is suggested by the anatomic studies of McGregor, but how often this actually occurs is unknown. Godard reported the case of a man, age 56, who wore a tight bandage over an interstitial type of ectopy which changed it to the perineal variety.

Complications—One would expect the same complications to occur in the perineal as in the other forms of undescended testes. Franz reports an instance of epididymitis in a male, age 24, with a left perineal testis, but whether there is a greater predilection for the ectopic organ is unknown.

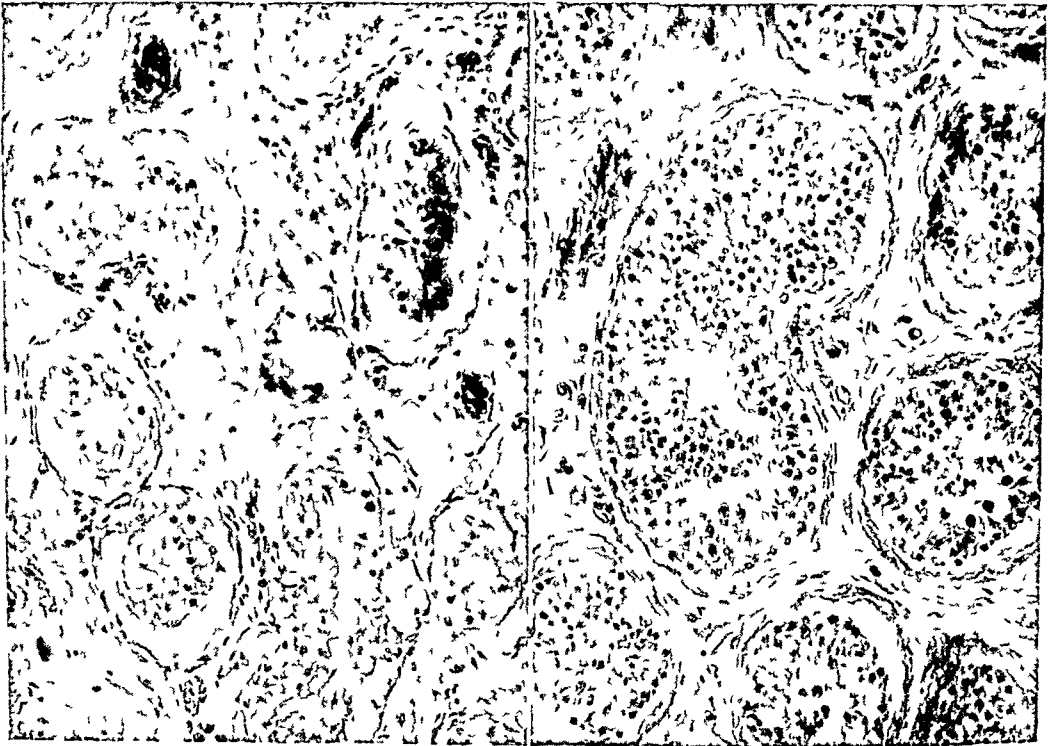


FIG 1—Case 1 (Path No A 36 2056) Left perineal testis in man age 54. Photomicrograph showing marked degenerative changes in seminiferous tubules with hyalinization, increase in fibrous interstitial tissue. No spermatozoa ($\times 150$)

FIG 2—Case 1 (Path No A 36 2056) Right descended testis. Photomicrographs showing testis to be normal except for slight disorganization ($\times 150$)

No instance of malignancy of a perineal testis has been reported in the available literature, probably because too few cases of perineal ectopy have been reported.

Histology—Sonneland, in 1924, could find no histologic study of a perineal testis. Even at the present time, no mention of the minute anatomy of such organs can be found in the available literature. McGregor states that the perineal testis is usually of normal size and development. This statement is surprising, knowing from clinical and experimental studies how atrophic the testis becomes when deprived of its scrotal environment. From a histologic point of view, the appended case reports are instructive.

THE PERINEAL TESTIS

Case 1—No UH 621277 R P, age 54, was admitted to the University of Minnesota Hospitals October 9, 1936. He had been treated in the Out-Patient Clinics for a chronic duodenal ulcer, tabes dorsalis, and a neurogenic vesical dysfunction. He had been receiving antisyphilitic therapy, and had followed a medical regimen for the duodenal ulcer. Because of marked pyloric obstruction and epigastric pain, he was referred to the hospital, where a posterior gastro-entrostomy was performed, from which he died.

Physical Examination—The patient had a perineal testis. He had no symptoms referable to this abnormality. The perineal testis was situated on the left side near the scrotal-thigh juncture, and could be pushed posterior to the scrotum near the median raphe and anteriorly in front of the pubic bone. It measured 3 by $2\frac{1}{4}$ by 2 cm. There was a left indirect inguinal hernia, the spermatic cord was not definitely felt on the left. The scrotum was atrophic on this side. The right testis was normal in size, shape and position and measured $4\frac{1}{2}$ by 3 by 2 cm.

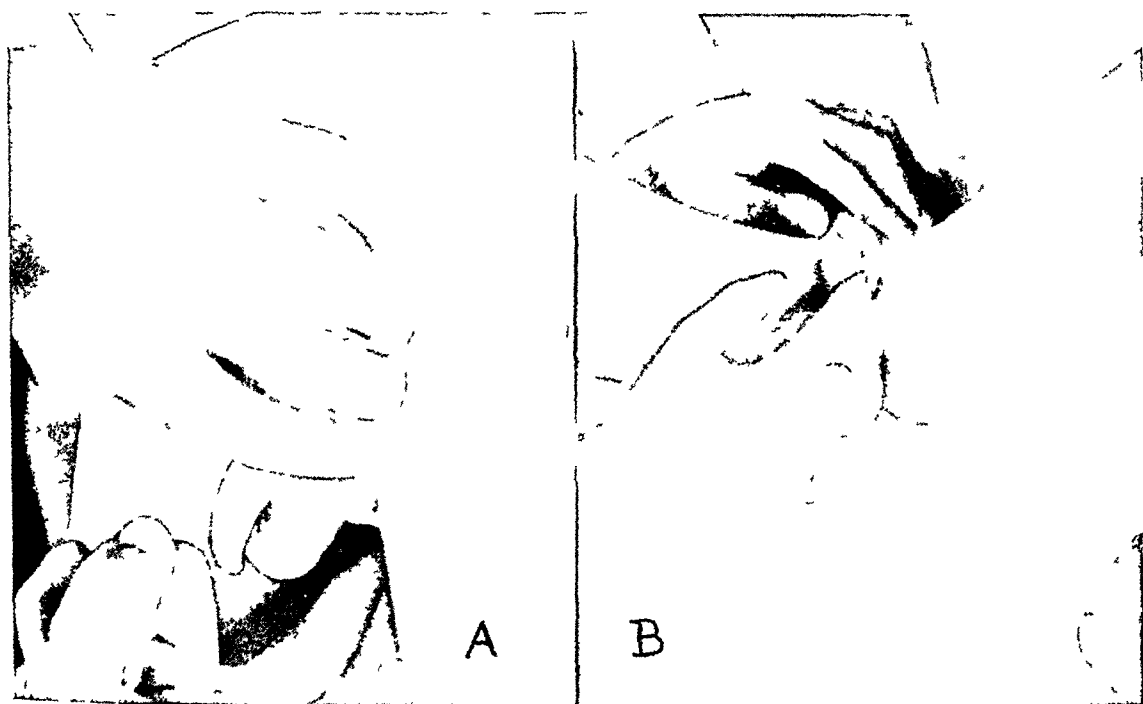


FIG 3 A and B—Case 2. Left perineal testis in boy, age six. The testis has been pushed up toward inguinal region. Note atrophic scrotum on left side.

Autopsy Report—The right testicle weighed 23 Gm and the left 8 Gm. The left testis was definitely atrophic in appearance. The relationship of the epididymis and testis was normal. The tunics of the ectopic gonad were thickened. Microscopically (Path No A-36-2056), the perineal testis showed marked degeneration of the seminiferous tubules, no spermatogenic cells were seen. There was an increase in the interstitial tissue (Fig 1). The right testis was fairly normal in appearance except for some disorganization of the germinal epithelium probably the result of the patient's terminal illness (Fig 2).

Case 2—No UH 632363 E B, age six, was admitted to the Out-Patient Pediatric Clinic with a left indirect inguinal hernia and a left perineal testis. Past history was essentially negative except that the child had been operated upon at two weeks of age for pyloric stenosis (Rammstedt operation).

Physical Examination revealed that while the right testis was in the scrotum, the left testis lay under the skin in the perineum, it could, however, be pushed between the scrotum and thigh to the left inguinal ligament. The testes were the same size and measured $1\frac{1}{4}$ by 1 by 1 cm. The patient's mother said that at no time had there been symptoms referable to the ectopic organ (Figs 3A and B). The patient was referred to the hospital for a left orchiopexy.

Operation—October 26, 1937 The procedure employed was Wangenstein's modification of the Keetley-Torek operation. A vaginal type of congenital hernia was present. A fibromuscular band of tissue about 4 cm long (the gubernaculum) extended from the lowest portion of the hernial sac and testis and spread out into the fibrous tissue in the scrotal-thigh juncture. From the external ring the testis could be pushed over the inguinal ligament along the scrotal-thigh juncture almost posterior to the scrotum. The scrotal neck was stenotic and closed over by fibrous tissue. Definite evidence of reduplication of Colles' fascia in this region, as McGregor described, was not seen.

There was a slight separation of the testis and epididymis and an appendix testis was present. The ectopic testis measured 1 by $3/4$ by $3/4$ cm. The tunics were not thickened.

A biopsy of the testis (Path No HO-37-3214) showed small seminiferous tubules separated by a loose connective tissue stroma. The lumina of the tubules were obliterated by two to three irregular layers of darkly staining epithelial cells. The whole appearance was that of a prepubertal testis, not unlike that which one would find in the normally descended testis of a boy of the same age (Fig 4).

Treatment—The treatment of the perineal testis is surgical. While most patients with undescended testes may have the operation deferred until the ninth to eleventh years, patients with perineal testes probably should be operated upon earlier, as the chance of trauma to the ectopic gonad would seem to be greater. The use of gonadotropic hormone is not indicated, because further descent will not improve the aberrant position, the value of using this substance to increase

the size of the prepubertal perineal testis may be questioned. The treatment of choice in this condition is orchiopexy.

SUMMARY

That the perineal testis is a rare anomaly is evident since only slightly more than 100 cases have been thus far reported. No mention of the histology of such organs has been found in the available literature.

Two cases of perineal testes are presented. A histologic study of these two testes revealed the usual picture incident to cryptorchidism. In the man, age 54, the perineal testis showed the atrophic changes commonly seen in old, untreated undescended testis, in the young boy, age six, the ectopic testis had

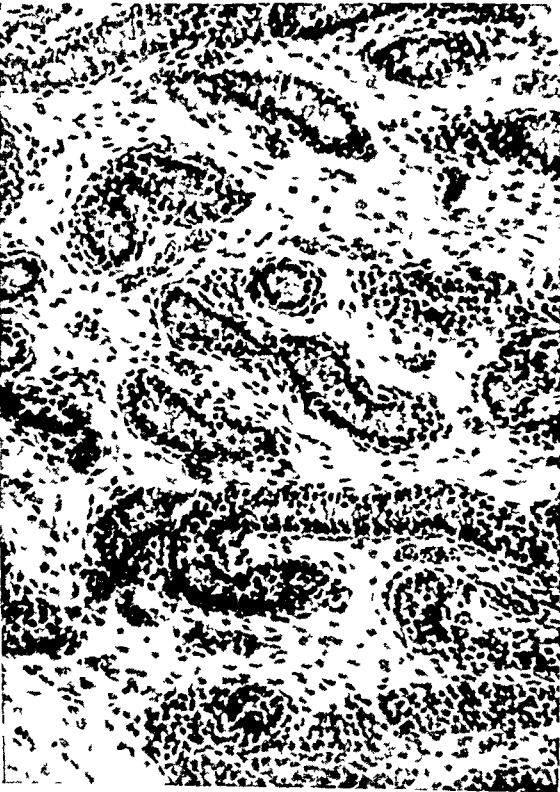


FIG 4—Case 2 (Path No HO 37 3214) Photomicrograph of a section of the perineal testis shown in Fig 3. The appearance is not unlike that seen in normally descended prepubertal testes of patients of same age ($\times 150$).

the appearance of a prepubertal gonad, indistinguishable from that of a normally descended testis in a patient of the same age

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EFFECTS OF LIGATIONS ON NERVES OF THE EXTREMITIES

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IT HAS been shown in other papers that ligations of the limbs result in an instructive form of shock, and also that the resistance to local asphyxia is greater than is commonly supposed, since the limbs of animals can survive complete lack of circulation for at least 15 hours, and the same is presumably true for man. Granting a proper form of tourniquet applied without excessive tension, the danger of gangrene under ordinary surgical conditions is largely imaginary. Certain other sequelae are of surgical interest, however, particularly, the occasional paralyses or contractures. Only two possible causes for such lesions exist—namely, pressure in the zone of ligation, and asphyxia. Experimental observations favoring each of these causes will be discussed.

Trauma of Tourniquet—(1) In rats, brief ligations of a hind leg for five to 20 minutes cause varying degrees of injury, the motor manifestations ranging from slight lameness to complete paralysis, while the responses to sensory stimuli indicate different grades of obtunded sensibility rather than anesthesia. The rabbit shows less effect than the rat, and the dog and cat are still more resistant, so that their legs can be ligated for several hours with comparatively slight nervous effects. Rather than to assume that the tissues of the larger species are less sensitive to asphyxia, it is more rational to consider that their tougher structure makes them more resistant to pressure of the tourniquet.

(2) As the ligations of the rat's leg are lengthened beyond 20 minutes, the nervous effects increase, so that after 40 minutes there is complete paralysis and anesthesia. There is no increase of degree when the time of ligation is increased to as long as ten hours, but there is a marked and progressive increase of duration. After the 40-minute ligation, the nerve functions may return within a day or two, but after the longest ligations the recovery is delayed for several weeks, as will be shown later. This recovery is plainly the result of regeneration of nerves, because its progress is traceable from above downward. If the nerves must regenerate after being killed by asphyxia, it is difficult to see why the process should be more rapid after a three-hour ligation than after a ten-hour ligation, but it is a reasonable assumption that more severe and prolonged damage will result in the zone of ligation after ten hours than after three hours. Similar results are found in the larger species.

(3) Comparatively brief ligations, from 15 minutes up to two hours, when suitably repeated over a series of days, increase both the degree and

the duration of the paralysis, which in some instances has taken as long as two months to clear up

Asphyxia—(1) When a small hole is dissected through the upper leg, so that one rubber ligature can be passed through on one side of the sciatic nerve, and another ligature on the other side of the leg, it is possible to ligate all structures of the leg except the nerve, and the usual paralysis is still obtained. A partial objection can still be made that the nerve is damaged by an inflammatory process

(2) Ehlich and Biegele obtained prolonged paralysis of the hind legs, bladder and rectum by clamping a rabbit's aorta just posterior to the renal arteries for 45 to 60 minutes. The writer has duplicated this experiment, but a simpler way of obtaining the same result is by binding a heavy rubber band tightly around the lower abdomen of a semi-anesthetized rat or rabbit. In a large number of such experiments performed upon rats, the more detailed findings were as follows. One hour is about the longest safe period, strong rats will often endure one and one-half hours, but two hours or longer cause rapid death from shock. The impairment of defecation may continue for a couple of weeks but is seldom dangerous, occasionally it is responsible for fatal fecal obstruction. The bladder paralysis, accompanied by prostatic swelling, results in the death of all male rats within about a week, from urinary retention, with accompanying hydro-ureter and hydronephrosis. Female rats, however, recover, and the paralytic urine retention and dribbling pass off in about two weeks. Other results are illustrated in the following summary of a typical protocol

Experiment 1—Ligation of a rat's abdomen for 45 minutes was followed by complete paralysis and anesthesia of rear parts, but within three hours sensation was again present in hind legs and tail. Perfect sensory function continued, but motor paralysis remained complete until curling movements of the tail (voluntary or reflex) were noticed on the fifteenth day. Four days later a very slight use of the hind legs began, and increased steadily to normal locomotion, ten days later (29 days after ligation)

In this experiment, the spinal cord is evidently protected against pressure by its bony encasement, and is nourished by its own blood vessels. Also, if the paraplegia were due to destruction of the cord, regeneration would be impossible. The conditions are still clearer when the paralysis results from ligation of the aorta alone. Therefore, it is positively demonstrated that paralysis can be produced in the rat's legs by 45 minutes of asphyxia, uncomplicated by any local traumatism

It must be deduced from the above that paralyzes due to destruction of nerves can be caused both by direct crushing and inflammation in the region of the tourniquet, and by asphyxia. It is possible for the direct tourniquet pressure to give rise to ulceration, necrosis, scarring and various permanent deformities, in all the animal species used. On the other hand, in hundreds of experiments performed for various purposes, there has never been a single instance of permanent damage when the paralysis was produced by asphyxia alone, without any local trauma. The animal experiments, therefore, indicate that asphyxial injury of nerves and also of the muscles (if not carried to the

point of gangrene) is always followed by complete recovery, that, therefore, the word "ischemic" is wrongly applied to permanent paralyses and contractures following the clinical use of the tourniquet, and that these effects are most probably attributable to direct trauma of the nerves and muscles under the tourniquet

Influence of Tension and Temperature—All the statements in this paper are based upon the use of a narrow rubber tourniquet, applied with just sufficient tension to stop the arterial blood flow. Obviously, excessive tightness of the ligature is a most provocative cause of damage to the nerves, vessels and all other tissues

Loose, partial, or "venous" ligations, which impede the venous return while permitting arterial inflow, may produce great congestion and edema and some degree of subsequent arterial hyperemia, but they do not cause paralysis or anesthesia, even when prolonged to eight hours or repeated over a series of days

The statements also apply to results obtained at comfortable room temperatures. All the effects of asphyxia, including the nerve degenerations, are greatly augmented or accelerated by heating the ligated part to febrile temperatures, and are likewise progressively retarded by cooling, down to a minimum close to 0°C , as described in other papers¹. It also seems reasonably certain that the effects of direct pressure of the tourniquet upon nerves and other structures are increased by warmth and diminished by cold, though data have not been collected for positive proof

Motor and Sensory Regeneration—As above mentioned, large numbers of experiments in rats have uniformly shown that sensation suffers less from ligation than muscular power. Since the two kinds of nerve fibers supposedly do not differ in physical resistance, and since they sometimes run in the same nerve trunks, it seems necessary to explain the different behavior as a distinct difference in sensitiveness to asphyxia

There is an equally distinct difference in the rates of regeneration. Special observations on several scores of rats yielded the appended data on the rate of recovery following different periods of asphyxia (Table I)

TABLE I

RATE OF RECOVERY FOLLOWING DIFFERENT PERIODS OF ASPHYXIA

Duration of Ligation	Results
$\frac{1}{4}$ to 1 hour	Increasing impairment, up to complete paralysis and anesthesia, but usually passing off within a day or two
2 to 3 hours	Shortest recovery of sensation in 4 days, of muscular movement in 12 days. Latest recovery. Only partial return of sensation in 23 days with paralysis still complete
4 to $4\frac{1}{2}$ hours	Recovery of sensation in 18 to 22 days, of muscular movement in 4 to 6 weeks
5 to $6\frac{1}{2}$ hours	Recovery of sensation in 16 to 24 days, of muscular movement in 5 to 6 weeks
8 to 9 hours	Sensation evident in 3 to 4 weeks, but apparently blunted. Recovery of muscular movement in 7 to 8 weeks

Comparative Resistance of Nerve Fibers and Cells—At the time of publishing (1919, 1922) the experiments with clamping of the pancreatic vessels, the writer² was only partially acquainted with the literature of asphyxial effects upon nerve cells, and, therefore, had some hopes of obtaining totally denervated organs by stopping the blood supply long enough for all nervous elements to degenerate while the glandular tissues survived. It was a surprise to find the numerous intrapancreatic ganglia in excellent condition microscopically after asphyxia for as long as two hours, the impression arrived at was that the nerve cells could survive fully as long without circulation as the epithelial cells. This observation has since been learned to be in harmony with those of earlier investigators.

The earliest tests (Mayer,⁷ 1878) showed that brain functions could not be restored after the carotid and vertebral arteries had been clamped for ten minutes. Batelli³ extended this time to 15 minutes in some instances, when the circulation was arrested at the heart or aorta. The findings of Stewart, Guthrie, Burns and Pike¹¹ were confirmatory. Others (Ehrlich and Brieger⁵, Spionck¹⁰, Sarbo⁸, Gomez and Pike⁶) proved that the small pyramidal cells of the cortex were the most sensitive, being killed in eight minutes, while the Purkinje cells break down after 13 minutes. The cells of the medulla require 20 to 30 minutes of anemia before the damage is irreparable. The cells of the spinal cord and spinal ganglia survive asphyxia up to 45 or possibly to 60 minutes. The cervical ganglia (Tuckett,¹² Schroeder⁹) retain structure and function after more than 60 minutes, being more resistant than the cells of the central nervous system.

Cannon and Burket demonstrated that when the blood supply of portions of intestine is completely ligated off for six or seven hours, the ganglion cells of the myenteric plexus still retain normal microscopic appearance and functional capacity. They point out the importance of this remarkable resisting power in relation to hernia, intussusception and other accidents involving temporary anemia. If, instead of ligation, the anemia was produced by broad pressure between two plates of glass, the nerve cells could survive for only three and one-half hours, and, furthermore, the smooth muscle tissue suffered round cell infiltration and partial replacement by fibrous tissue. Whether the reason is because of the more complete pressing out of blood, as Cannon and Burket⁴ seem to imply, or a displacement of lymph and tissue fluids, or direct injury of the cells by pressure, the use of glass plates seems to be comparable to the employment of wide tourniquets of any type. As mentioned elsewhere, the prevalent surgical practice of tying for a wide distribution of pressure is, according to experimental evidence, not as gentle and conservative of tissue vitality as has been supposed, but is actually more destructive than a narrow ligature, provided the pressure in each instance is just sufficient to stop the blood flow.

These results, showing no serious damage to ganglion cells after six or seven hours of ligation, may be compared with those previously described, in which motor and sensory paralysis of the limbs was obtained after much

shorter ligations. The comparison is best made with the experiments in which paralysis of the hind legs of rats and rabbits resulted from about an hour of stoppage of circulation in the abdominal aorta, so that any mechanical traumatism of the leg nerves by the tourniquet is excluded. The conclusion seems apparent that the peripheral nerves are more resistant to asphyxia than the cells of the central nervous system, but less resistant than sympathetic ganglion cells. Careful attention should be paid to possible differences between species before drawing such conclusions too positively. The temperature during ligation is also a most important factor. Since the myenteric plexus retains its function after the ligations mentioned, there must be a survival of the fibers as well as the ganglion cells. In the leg ligations, no anatomic studies have been made to determine whether the sympathetic fibers degenerate along with the motor and sensory fibers, in which case the prolonged hyperemia must be strictly paralytic in character, or whether all the sympathetic fibers survive, or only the vasoconstrictors degenerate, so that there may be a nervous element in the vasodilatation. There is a very obvious teleologic reason for the high resistance of peripheral ganglion cells, because of the chance of their being exposed to anemia for periods which would kill central nervous cells and because of the irreparable damage resulting from their loss. There is no such teleologic reason for resistance on the part of the fibers, because they can regenerate, but it is physiologically difficult to comprehend survival of the cell bodies under conditions which kill their neuraxes. If the contrast exists between the entire sympathetic neurone and the entire cerebral or spinal neurone, or between preganglionic and postganglionic fibers, there may be a useful experimental opportunity to free an organ from part or all of its innervation by means of suitable asphyxia. It may also be inquired whether the different resistance of central and peripheral nerve cells, or of motor, sensory and sympathetic nerves is connected with differences in the activity of their metabolism or with other causes. The entire question of differences in resistance to anemia is therefore interesting but unsettled.

CONCLUSIONS

(1) The nerve lesions resulting from ligation of limbs may be caused either by direct pressure of the tourniquet or by asphyxia. The experimental evidence suggests that permanent paralyses arise only from the former cause. It further suggests that wide pressure is more injurious than a narrow band.

(2) The duration of the nerve paralyses increases in proportion to the time of ligation, as illustrated by a schedule of the periods required for recovery in the legs of rats after graded periods of ligation.

(3) The tension of the tourniquet, and the temperature during ligation, are important factors in the after-effects.

(4) Motor and sensory nerves differ in their sensitiveness to asphyxia, in that the former suffer paralysis much more readily and also regenerate more slowly.

(5) These experiments, together with the existing literature, show that

peripheral ganglion cells are enormously more resistant than the fibers of cerebral or spinal nerves. Numerous details concerning the comparative resistance of various nerve cells and fibers are undecided.

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ACUTE HEMATOGENOUS BURSTITIS

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ACUTE bursal infections of metastatic origin are rare complications that may arise in the course of, or as sequelae to, the acute infectious diseases, septicemias, or as secondary, metastatic lesions in pulmonary, otitic, upper respiratory, dental, or dermal suppuration.

The onset may be insidious or sudden, with chills, fever and prostration. The local lesion makes its presence known by localized pain over a joint, slight swelling, limitation of movement due to pain and muscle spasm. Before the inflammatory exudate is of sufficient amount to distend the sac, the condition may be mistaken for acute infectious arthritis, or osteomyelitis. As the disease progresses, however, the inflamed bursa may become clearly outlined and palpable. Undoubtedly, deep seated bursitis in any location is more often overlooked than recognized. A knowledge of the location, extent, and possible pathology of bursae may, in many cases of unyielding inflammation, explain the obscure pain about such regions as the hip, shoulder or knees. Bursitis should always be considered in deep seated abscesses of obscure origin, especially in the neighborhood of the buttock.

Metastatic bursal abscesses may occur at any age, but the disease is more common in adults. Purulent effusion in the subacromial bursae was observed by the writer in two infants suffering from gonococcus bacteremia. Incision yielded pus which on culture showed the gonococcus.

Boissonas and Kummer¹ quote A. Martin who, in 1929, reported a number of cases of suppuration in the muscles, synovia, joints and bursae, following varicella. One case showed suppuration of the trochanteric bursa and one of the retro-olecranon bursa. Recovery occurred after incision and drainage.

J. M. Hitzrot² reported three cases of infectious, calcific subacromial bursitis. In one, a hemolytic *Streptococcus*, originating in a tooth, a sinus in another, and a hemolytic *Staphylococcus aureus* in an ulceration of the cervix, were recovered in the exudate evacuated at operation. Hitzrot observed another case of suppurative bursitis involving the bursa, over the coracoclavicular ligament, which appeared in a man three weeks after mastoidectomy secondary to pneumonia. Incision yielded pus, which on culture showed a *Streptococcus*.

B. S. Barnes³ reported two cases of suppuration of the shoulder, one of these involving the subacromial bursae. The patient was a woman, age 35, who suffered from a *Streptococcus* septicemia, secondary to an induced abortion. During the course of her illness, the left shoulder became involved and

a large collection of pus was evacuated from the subacromial bursa. Blood and smear cultures showed the presence of hemolytic Streptococci.

Codman⁴ considers acute suppurative subacromial bursitis a rare lesion. In 1,151 various shoulder lesions, he saw only one suppurating acute case from pathogenic bacteria. Even this case was doubtful, and was probably to be explained by contamination of the culture.

Weeks and Delpart⁵ stress the importance of focal infection in cases of subacromial bursitis. Acute symptoms may occur after a period of rest and without immediate antecedent trauma.

In their cases, some upper respiratory infection, such as cold, influenza, or abscessed teeth, usually preceded onset of shoulder pain. They do not make any references to acute suppurative lesions in their communication.

L. Carp⁶ reported eight cases of radiohumeral bursitis, but none of these was of the infectious type. One case was operated upon by Dr. S. Kleinberg. The bursal cyst contained a milky fluid, which on culture was negative. Microscopic examination revealed thickened inflammatory tissue, foreign body giant cells, and irregular deposits of calcareous material.

Lasher and Mathewson,⁷ writing upon olecranon bursitis, state that frequently at the time of an injury superficial abrasions or lacerations of the skin occur. These afford a portal of entry for low grade infections, and the synovial fluid in the distended bursae becomes an excellent culture medium for the slow proliferation of invading organisms. The occurrence of osteomyelitis is almost an invariable complication when the bursa is distended with pus. The type of lesions these authors describe was due to local penetration of bacteria. Their cases were not of metastatic origin.

Six cases of metastatic bursal abscess form the basis of the present communication. The subacromial bursa was involved in four patients, the gluteal and prepatellar in two.

The disease occurred as a complication in two cases of acute mastoid suppuration, in two cases of pulmonary suppuration, and in one case of Staphylococcal septicemia, secondary to carbuncle. In one case of purulent subacromial bursitis, we did not ascertain the origin of the abscess. Blood cultures were positive in two patients. In the cases of otitic origin, smear studies of the discharge from the ear and evacuated bursal pus, similar organisms were isolated—pneumococcus Type 3, and hemolytic Streptococci. Patients with positive blood cultures revealed identical organisms in the bursal pus—hemolytic Streptococci and hemolytic *Staphylococcus aureus*.

Needling was employed in all cases as a diagnostic measure. This verified the diagnosis of abscess in all but the case of gluteal bursitis. In this case an early diagnosis was not made. Spontaneous rupture occurred six weeks after onset of the disease.

SUPPURATIVE SUBACROMIAL BURSITIS

Case 1—P. R., male, age 62, was admitted February 20, 1936 to Mt. Sinai Hospital, for treatment of acute mastoiditis of four weeks' duration. Roentgenologic ex-

amination revealed a cloudy mastoid with ill-defined and decalcified cellular structures. Temperature, 99.2° F, blood pressure, 150/75. While the ear condition represented the major lesion, the patient had also complained of pain and stiffness of the left shoulder for the previous three weeks.

Physical Examination The left ear revealed a profuse, yellow discharge, perforation of ear drum, and mastoid tenderness. Heart, lungs and abdomen were negative. The left shoulder joint was painful, tender and stiff. Movements were restricted by muscle spasm. No effusion was demonstrable in the joint or subacromial bursa.

Laboratory Data Blood count Hb 92, R B C 4,700,000, W B C 12,300, large lymphocytes 26, transitionals 2. Urea nitrogen 23.3. Blood sugar 140. Urine faint trace albumen, occasional W B C and hyaline casts.

Operation—February 20, 1936. Mastoidectomy was performed under general anesthesia. Extensive necrosis necessitated removal of considerable bone. During course of operation, the lateral sinus was accidentally opened, requiring packing to check the hemorrhage.

Postoperative Course Five days after operation, the patient developed a chill, temperature rose to 103° F, pain in the shoulder became accentuated, fluctuation over subacromial bursa was demonstrable. Roentgenologic examination revealed slight erosion of greater tuberosity and anatomic neck of humerus. Blood culture was negative. Diagnostic bursal tap yielded bloody pus. Under local anesthesia, a two inch, linear incision was made over the upper arm, the fibers of the deltoid muscle were separated, and a copious purulent collection in the subacromial bursa evacuated. Finger exploration failed to reveal any perforation in bursal floor. Smear and culture studies from ear and bursa revealed pneumococcus Type 3. Systemic and local symptoms promptly subsided following above procedure. Complete functional restoration of the involved shoulder was obtained in six weeks.

Case 2—D M, male, age 33, was admitted to Mt Sinai Hospital November 16, 1937, with chief complaint of pain and stiffness of left shoulder, low back pain and a sciatic syndrome. These symptoms were attributed to an injury sustained two weeks previously. Prior to this admission, the patient had been in the hospital in a critical condition for about three months, having been discharged September 26, 1937. Beginning with a carbuncle on his upper back, he had developed a severe hemolytic *Staphylococcus aureus* septicemia. During the course of this illness, the following complications were noted: five lung abscesses, hepatitis, empyema, atelectasis, metastatic skin abscesses and a renal carbuncle. It is interesting to note that the bones and joints escaped the infection at this time. Therapy consisted of surgical drainage of the carbuncle, transfusions, hemotherapy, antitoxin vaccine and bacteriophage. The patient improved generally under symptomatic treatment and measures to build up his general condition. On leaving the hospital, he was asymptomatic and continued to improve until the onset of the present illness. The injuries were treated as sprains, but did not respond to rest and physiotherapy.

Physical Examination on admission revealed an emaciated, debilitated, anemic young man. Temperature 102° F, pulse 100, respirations 24. The left shoulder was painful, the surface temperature was elevated, and tenderness was elicited upon pressure over the greater and lesser tuberosities. Slight fluctuation was demonstrable over the subacromial area. Rotation and elevation of the shoulder were restricted by muscle spasm. Examination of back revealed spasm of the erector spinae, pain on movement and percussion over lumbar vertebrae, and restricted straight leg-raising on left side. Heart, lungs and abdomen were negative. Leukocytosis 12,600, 79 per cent polymorphonuclears. Blood and casts were found in the urine. The temperature was of a septic type. Blood cultures were negative. Roentgenologic examination of left shoulder showed thickening of cortex along mesial aspect of left humerus, the spine showed a narrowed fifth lumbar intervertebral space, and prolapse of nucleus pulposi into the fourth and fifth lumbar vertebrae. Diagnostic bursal tap yielded seropurulent material which on culture showed

ACUTE HEMATOGENOUS BURSITIS

hemolytic *Staphylococcus aureus* On December 2, 1937, drainage of the subacromial bursa was instituted and bloody pus evacuated Finger exploration revealed a few fibrous strands beneath the acromion and tabs on the floor of the bursa Perforation through the floor was neither observed nor felt Systemic and local symptoms promptly subsided following operation A plaster of paris jacket was applied to immobilize the spine, and the patient was discharged December 5, 1937 in care of his physician

Case 3—U K, male, age 65, was admitted to the Mt Sinai Hospital Clinic December 21, 1937, with a painful, swollen, stiff right shoulder, of sudden onset, unknown etiology, and of five days' duration

Physical Examination revealed a well developed Russian, with advanced peripheral arteriosclerosis, dental caries and diseased tonsils Owing to language difficulties, a



FIG 1—Case 4 Showing the external contour of the effusion in the left subacromial bursa

clear idea of his previous medical history could not be obtained Temperature 100° F, pulse 90 The right shoulder presented an enormous effusion in the region of the subacromial bursa, as evidenced by the marked roundness of the shoulder and fluctuation beneath the acromion process Aspiration yielded thick, creamy, greenish pus, which on culture and smear examination was negative for T B, or other organisms Under novocain anesthesia, a two inch, linear incision was made below the acromion process Upon separating the fibers of the deltoid, the tense bursal wall was noted Incision yielded a copious flow of flaky, greenish pus Finger exploration revealed a roughened floor, but capsular tears, villi, or tabs were not present The peripheral termination of the bursa was located about three inches below the upper end of the humerus Rubber dam was inserted for drainage The patient did not return for further treatment

Case 4—J B, male, age 52, was admitted to the Mt Sinai Hospital October 30, 1937, complaining of pain and swelling of the left wrist and left knee, cough, and loss of weight Three months prior to admission, the patient had developed a cough, following an acute upper respiratory infection The cough was productive and associated with chest pain On one occasion, blood specks were noted Ten days before admission, he developed pain and swelling of left knee and left wrist

Physical Examination revealed an emaciated, middle-aged white male, with herpes labialis, coated tongue, and congested pharynx. Chest revealed bubbling rales at left base. Heart showed slight enlargement, irregular cardiac rhythm and poor tone. Left knee was swollen, painful, and flexed. Left wrist and hand were swollen, movements restricted and painful. Temperature was moderately elevated, and irregular, fluctuating between 99° and 101° F. Blood culture showed the presence of hemolytic *Streptococci*. Roentgenologic examination of the chest revealed enlarged heart, right hilar mass and normal knee and wrist joints. Under sulphanilamide therapy, 15 grains four times daily, the joint symptoms subsided and the blood culture became negative. The patient subsequently developed a very large pericardial effusion, which was repeatedly tapped during the following six weeks. The total amount withdrawn was approximately 6,500 cc. On December 15, 1937, a painless effusion was noted in the subacromial bursa of the left shoulder (Fig 1). Abduction and rotation of this joint were restricted by contracture of scapulohumeral muscles. Aspiration of the subacromial bursa yielded bloody pus. Under local anesthesia, a two inch, linear incision was made over the shoulder, the fibers of the deltoid muscle separated, and a tense distended subdeltoid sac was revealed. Incision resulted in evacuation of a considerable amount of pus. Finger exploration revealed a smooth bursal floor with no apparent perforation through the capsule, the wall itself was thick and congested. Culture of the pus removed revealed a hemolytic *Streptococcus*—the same organism which had been responsible for the septicemia earlier in the course of the disease. Roentgenologic examination of the left shoulder showed evidences of erosion and absorption of the greater tuberosity of the head of the humerus. This patient is still in the hospital with the cardiac condition. He has at the present time an adhesive pericarditis which interferes markedly with the circulation. An operation has been considered to relieve this condition. Range of motion of the shoulder is still greatly limited.

HEMATOGENOUS, SUPPURATIVE PREPATELLAR BURSITIS

Case 5—S. C., male, age 70, was admitted to the Northern Liberties Hospital September 28, 1935, complaining of pain in the right ear of ten days' duration, pain in the right knee, fever, and prostration. Temperature 105° F, pulse 130, respirations 30. Two days before admission, a paracentesis of the right ear was performed, resulting in a discharge of pus.

Physical Examination revealed an obese male, B. P. 160/80, cardiac decompensation, moist râles in both lungs, enlarged liver and a swollen, painful right knee. Roentgenologic examination of the right ear revealed a cloudy mastoid with thinning and absorption of the cells and a thickening of the anterior wall of the lateral sinus, the right knee was negative. W. B. C. 15,800, polymorphonuclears 95 per cent, R. B. C. 4,150,000, Hb 77 per cent. Blood sugar 133, blood culture sterile, Wassermann negative. A swollen prepatellar bursa was recognized October 3, 1935, which yielded thick creamy pus on aspiration. The bursa was incised and drained. Following this procedure, the temperature which had been of the septic type gradually dropped to a lower level. This patient remained in the hospital for about one month. His ear symptoms gradually lessened. No radical procedures upon the mastoid were attempted, owing to his desperate condition. Smear studies from ear discharge and knee revealed a hemolytic *Streptococcus*.

HEMATOGENOUS SUPPURATIVE GLUTIAL BURSITIS

Case 6—M. A., female, age 27, married, was admitted to Mt. Sinai Hospital October 18, 1936, complaining of chills, fever, prostration, and severe pain in the left buttock of eight days' duration, sudden in onset, and attributed to exposure to cold and wet. Except for bronchiectasis, her previous medical history was irrelevant. She had had three children, the last having been born two and one-half months ago.

Physical Examination revealed a well-developed woman, acutely ill, temperature of

103° F, pulse 130, respirations 28, and an acute inflammatory process involving either the left ilium or hip joint, and chronic pulmonary pathology (bronchiectasis). Objective findings were marked tenderness over a limited area in the left buttock about four fingerbreadths below the crest of the left ilium, and one fingerbreadth lateral to the outer border of the sacrum. Flexion of either extended leg upon the abdomen accentuated the pain in the right buttock. The upper extremity of the thigh, in the trochanteric region, was not tender to pressure. There was no demonstrable swelling in this region.

Vaginal examination revealed no abnormality other than a cervical discharge. Rectal examination was negative. Roentgenologic examination following a barium enema revealed a normal colon, the pelvis and left hip joint were negative except for a small area of increased density, suggestive of a calcium deposit in the soft structures of the left buttock. RBC 3,450,000, WBC 15,500, polymorphonuclears 84 per cent, small lymphocytes 13 per cent, Pr 3, Hb 74, urea nitrogen 15.8, blood sugar 99, Wassermann, Widal and complement fixation for gonococci negative. Urinalysis: Faint trace of albumen, few WBC and RBC, no casts. Blood culture was sterile. Although the roentgenograms were negative for bone pathology a provisional diagnosis of acute osteomyelitis of left ilium was made, and the patient was treated expectantly for three weeks. During this period, the pain in left buttock persisted, temperature fluctuated between 99° and 101° F, and the pulse rate was accelerated, ranging between 100 and 120. She received several blood transfusions, supportive measures and sedatives. On one occasion aspiration of the right buttock resulted in a dry tap. A plaster of paris encasement was applied October 26, 1937, but was removed a week later since it did not relieve the local symptoms.

Operation—November 4, 1937. The left ilium was explored through a large incision over the left buttock, exposing the sacro-iliac joint and ilium. Careful palpation and inspection failed to reveal any periosteal thickening or subperiosteal abscess. A tube drain was inserted into the lower angle of the wound. Following this procedure, the temperature became more elevated and assumed a septic type. Blood cultures continued to be sterile, and roentgenologic examination failed to reveal any bone involvement. The above symptoms persisted until November 26, 1937, at which time there occurred a spontaneous rupture of pus through the healed incision in the buttock. From then on she continued to convalesce satisfactorily and was discharged December 13, 1937, with a small draining sinus in the buttock. It is highly probable that the bronchiectasis was the primary source of infection, and that the gluteal abscess was a secondary metastatic manifestation of this condition. Antecedent trauma or other illnesses were not in evidence. Smear studies of the pus were not made.

COMMENT—Inflammation of the bursae beneath the gluteal muscles constitutes one of the most puzzling and frequently overlooked lesions in the vicinity of the hip joint. The acute syndrome simulates hip joint disease, osteomyelitis of the ilium, or acute septic arthritis of the sacro-iliac joint. The onset is acute, with high temperature, pain in the hip or buttock, and prostration. Pressure about the hip elicits exquisite tenderness, pain is accentuated by movements of the joint. Occasionally a sciatic syndrome is present due to pressure on the sciatic or gluteal nerves. Diagnosis of acute suppurative arthritis of the hip joint is usually made in these patients, and an arthrotomy performed. Thus an otherwise simple lesion is converted into a very serious condition, which threatens life or causes a permanent crippling disability.

In studying the anatomy of the buttock, we have been impressed with the large number of bursae which are located in this region. Spalteholz estimates the number to be from 10 to 30. According to Quain, among the more

important, constant bursa in this region is the large multilocular trochanteric bursa, and a number of smaller bursae connected with the gluteus medius and minimus, piriformis and ischium. J. E. Milgram³ has given us an excellent description of the connection between these bursae and the fascial planes of the thigh.

When the trochanteric bursa is affected there is tenderness over the great trochanter, and pain on movement of the limb. The extremity is flexed, abducted, and externally rotated. A resilient tumor develops posterior to the trochanter, underneath the aponeurosis of the gluteus maximus, which obliterates the hollow behind the trochanter. The gluteal fold may be effaced. In advanced cases, the purulent collection may spread along the fascial planes of the thigh, down to the external condyle. The finger-like prolongation of this bursa, which extends towards the sciatic nerve, may be involved, in which event severe pain down the leg may result.

Bursitis about the buttock, other than the trochanteric, is differentiated by the anatomic situation of the bursae, and by eliciting pain upon voluntary contraction of the muscle overlying the involved bursa. Four bursae, two under the gluteus medius, one under the gluteus minimus, and one at the edge of the piriformis, are closely associated, and particularly related to the summit of the trochanter. Symptoms point above the trochanter and are confined to the side of the pelvis, they may simulate osteomyelitis of the ilium. In these cases, the inflammation may give rise to deep-seated pain in the buttock, radiating down the leg, without any striking change in the contour of the buttock (Case 6).

In acute suppurations of the hip joint or osteomyelitis involving the upper end of the femur, all movements are restricted by painful muscular spasm. Jarring of the joint is painful. There is no swelling or tenderness of the buttock, but there is a fulness of the upper thigh. The capsule of the hip is distended and fluctuation may be demonstrable over its anterior aspect. Diagnostic tap is conclusive. Osteomyelitis of the ilium and suppurative arthritis of the sacro-iliac joint begin with a more violent onset, both locally and constitutionally. While roentgenologic examinations are valueless early in the course of these conditions, positive evidence becomes available as the disease progresses.

CONCLUSIONS

(1) Purulent collections in bursal cavities may occur as complications in the course of blood stream infections, and give rise to local symptoms which simulate septic arthritis or osteomyelitis. Case histories of six patients presenting these lesions are herewith recorded.

(2) A knowledge of the location, extent, and possible pathology of bursae is essential in differentiating these conditions from intra-articular or osseous lesions. The roentgenologic examination and diagnostic tap are the most reliable diagnostic procedures.

(3) Suppurative gluteal bursitis should always be considered as a diagnostic possibility in cases of deepseated pain in the buttock, associated with constitutional symptoms, and negative roentgenologic findings

(4) Incision and drainage are indicated when fluctuation is demonstrable

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CHROMICIZED BEEF TENDON FOR INTERNAL FIXATION OF FRACTURES ¹

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THE writer is familiar with the various methods of internal fixation of fractures, such as autogenous, osteoperiosteal, massive onlay, inlay and beef bone grafts and also the employment of pins or pegs, *etc.*, in and outside of the medullary canal, as well as pins, nails and plates used for the internal fixation of fractures, all of which have been used for internal fixation when it was considered they were indicated, and with which more or less good results have been obtained. However, the observations of Venable, Stuck and Beach¹ on the various types of metal used for internal fixation of bone and the accompanying electrolysis have caused me to question, somewhat, the employment of metal for fixation. Likewise, there have been many discussions both for and against all the methods and materials used in internal bone fixation. The whole question is, apparently, far from settled and, therefore, the new material herewith suggested may not be out of place.

Desiderata—Some four years ago, it occurred to the writer that it would be desirable to have a material that, as nearly as possible, possessed the qualities of an autogenous graft without the necessity of removing the graft from another part of the body and subjecting the patient to this additional surgery. It was realized that no material could be obtained that would reproduce bone. This material, therefore, could only act as a splint, should be properly sterilized and placed in glass tubes, should be absorbable, but should stay in place a sufficient length of time, and maintain reduction of the fracture long enough for union to get well started or be completed. The material should also be well tolerated by the tissues. It should be easy to work with, and come fashioned as a plate, cuff, pin or peg, as these forms of material are most acceptable to the majority of bone surgeons. It should be easily secured and of moderate cost.

Such a material could, apparently, only be procured from animals. The tendo achillis of the steer was considered to offer a structure of sufficient strength and proper histologic requirements. From the results obtained by Shipley with ox fascia, we were reasonably certain that this tendon obtained from the steer would be well tolerated by the tissues, if properly prepared.

Chromicized beef tendon was, therefore, prepared in plates, cuffs and pegs by a reliable manufacturer[†] of catgut products, sterilized and put up in glass tubes (Fig. 1). After working with this preparation, we found that it was

* Read before the Southern Surgical Association, at Birmingham, Ala., December 7, 1937.

† Davis and Geck, Inc., Brooklyn, N. Y.

absolutely sterile, easy to work with, did not show on a roentgenogram, would remain in position 60 to 90 days, had sufficient strength, and did maintain reduction of the fracture if properly introduced. It was well tolerated by the tissues and did not interfere with bone growth. We feel that 60 to 90 days is sufficient time for bony union to take place if it is going to occur, and that some type of splint, either of plaster or metal, should be used in conjunction with this material. We do not advise the use of chromicized beef tendon unless an open operation is indicated and when other, more simple methods have failed.

In using chromicized beef tendon we have followed the methods as out-

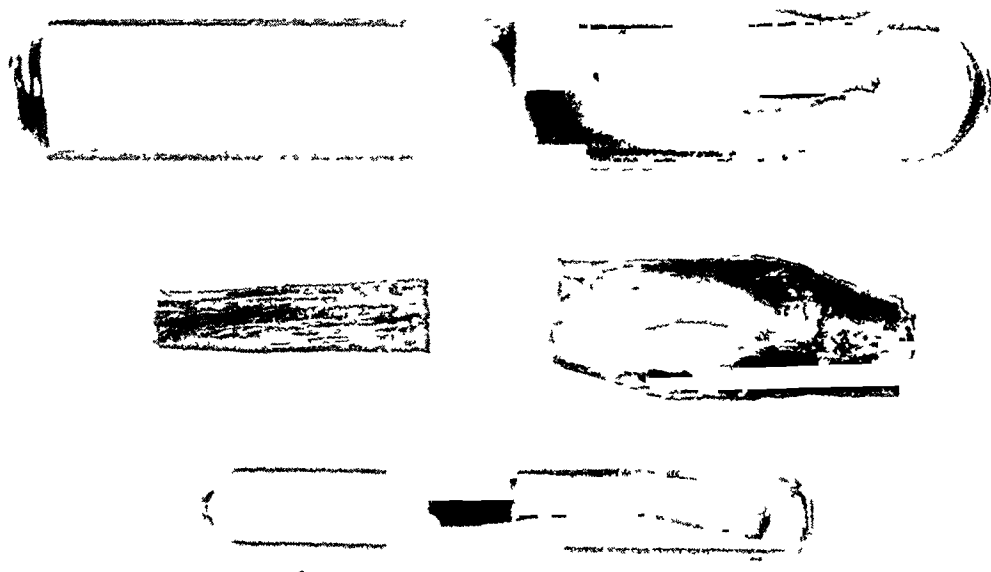


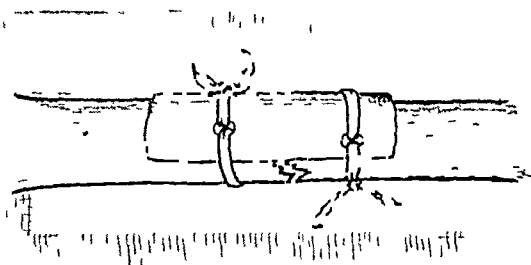
FIG. 1.—The appearance of both a peg and a cuff of the chromicized beef tendon as it comes in tubes

lined. The fracture having been exposed through a suitable incision, it is studied visually and the most desirable method of fixation is decided upon, as roentgenograms do not always give one an accurate idea of the fracture. The tendon is thoroughly washed in sterile water to remove all chemicals. If a cuff is to be used, it is placed over the periosteum and line of fracture, the ends of the latter having been first brought into proper alignment and held in position with any form of mechanical apparatus available. At either end of the cuff, holes are bored through it and the bone large enough to take a heavy kangaroo tendon suture. This suture is tied around the bone and over the cuff several times, thereby holding it firmly in position. The cuff should not extend over two-thirds of the circumference of the bone upon which it is being applied (Fig. 2). The blood supply should not be entirely excluded from the line of fracture. The cuff may also be formed into a roll for use in the medullary canal, the roll should not be a tight one so that it may permit the free circulation of fluids through it. This method overcomes most of the usual objections to materials placed in the medullary canal. Here also, holes are bored through either end of the cuff and bone, and the cuff is an-

choiced firmly in place with heavy kangaroo tendon firmly tied around the bone several times (Figs 3 and 4) On the large bones it may be necessary to use several cuffs or plates to secure firm fixation This is a matter of personal opinion and experience

The chromicized beef tendon pins or pegs are used in the same manner as bone or metal pins or pegs in oblique fractures (Fig 5), fractures of the

FIG 2



F. WIEGAND

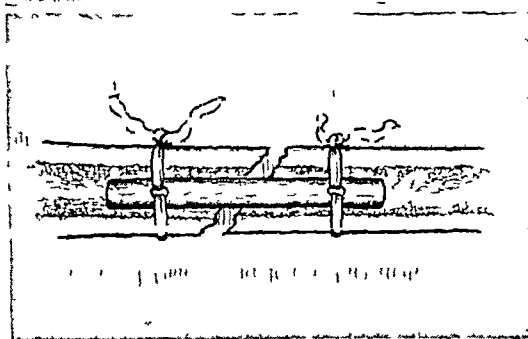
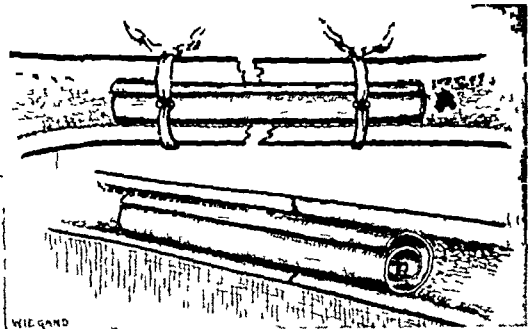


FIG 4

FIG 3



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F. WIEGAND

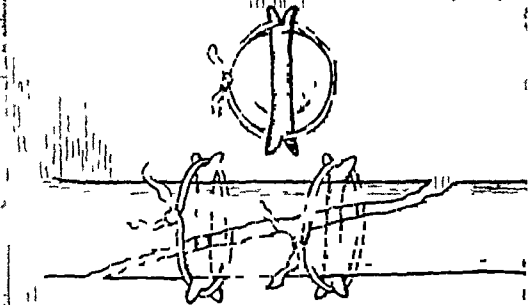


FIG 5

FIG 2—The appearance of the plate or cuff applied to the fracture and anchored in place by kangaroo tendon passed through holes bored through both the cuff and the bone

FIG 3—The appearance of the cuff rolled into a roll and placed in the medullary canal, and also anchored in position by kangaroo tendon passed through both the cuff and the bone

FIG 4—The chromicized beef tendon peg used in the medullary canal, illustrating, particularly, the loose fit of the peg

FIG 5—Illustrating the manner in which the pegs are passed through an oblique fracture with the ends split and anchored in position with kangaroo tendon

condyles or tuberosities (Fig 6), and fractures of the olecranon process (Fig 7), etc These pins or pegs may also be used in the medullary canal if desired It has been found that when these pegs are anchored in the medullary canal with heavy kangaroo tendon passed through holes bored through both ends of the tendon peg and the bone, it is not necessary for the tendon peg to fit the medullary canal tightly The tendon peg also has a certain amount of give or spring to it which permits it to be put in place more easily and without breaking These properties cause less damage to the endosteum, and also permit a free circulation of blood and serum around the peg When chromicized beef tendon pegs are used in oblique fractures, it is felt that it is a good idea to let the pegs extend beyond the bone on either side a short distance These ends can then be split with bone forceps and kangaroo tendon tied around the bone and through the split ends of the pegs, which will hold them in position and keep them from slipping in either direction (inset Fig 5)

Chromicized beef tendon can easily be cut with heavy scissors or bone cutting forceps. This permits the shaping of the peg or cuff without the use of motor saws, bone rasps, *etc*, thereby shortening the time of the operation considerably.

It is not claimed that chromicized beef tendon should be used in all fractures, but it is felt that it has a useful place in the armamentarium for bone surgery and in many instances can be employed to great advantage. We feel that it possesses many desirable qualities and is well worth consideration.

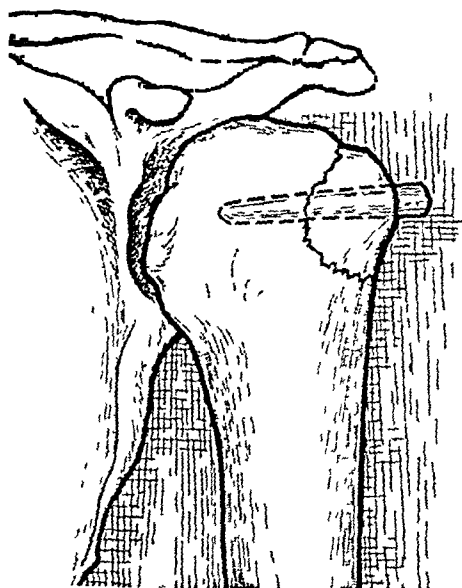


FIG 6—Showing the employment of the chromicized beef tendon peg for fixing fractures of the tuberosities

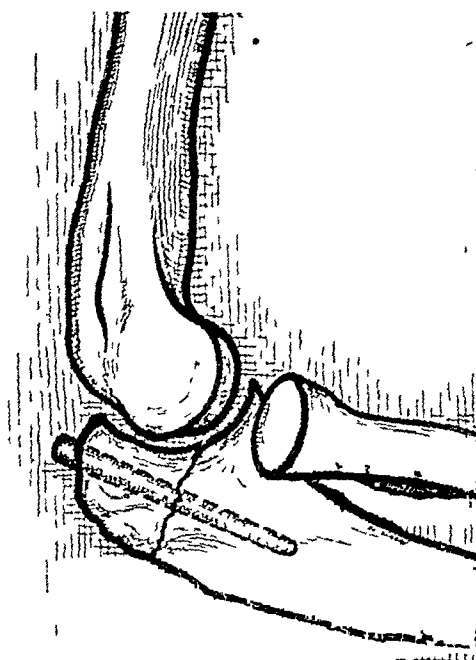


FIG 7—Showing the method of fixing a fracture of the olecranon with a chromicized beef tendon peg

ILLUSTRATIVE CASE REPORTS

Case 1—Female, age 35. Automobile accident. Complete separation of greater tuberosity of humerus, right arm, with anterior dislocation. Nailed beef tendon peg, Thomas splint, arm in abduction. *Result* Complete union in five weeks' time.

Case 2—Female, age 26. Automobile accident. Fracture of right olecranon. Complete separation and dislocation. Olecranon drilled and nailed, using beef tendon peg. *Result* Union, active and passive motion in five weeks' time.

Case 3—Male, age 32. Fracture of both bones of right forearm, middle third, caused by slate fall, and was unable to maintain alignment. Beef tendon cuff-type operation. Cuffs tied in place with chromic catgut. *Result* Union in six weeks' time. Bisected plaster encasement fixation.

Case 4—Male, age 40. Oblique fracture of left humerus, middle third, caused by slate fall, muscle between fracture line. Two beef tendon pegs were driven transversely and tied in position by kangaroo tendon. *Result* Union in seven weeks' time. Thomas arm splint applied.

Case 5—Male, age 28. Fractured first phalanx, right index finger. Labor accident. Intramedullary beef tendon peg used and finger splint fixation. *Result* Union in five weeks' time.

Case 6—Male, age 30. Automobile accident. Fracture of left femur, middle third. Muscle between line of fracture. Application of two beef tendon cuffs. Applied Thomas leg splint, and walking caliper. *Result* Union in ten weeks' time.

Case 7—Male, age 15 Fracture of both bones, left forearm middle third Unable to maintain proper reduction Beef tendon cuff applied to both radius and ulna, anchored in place by kangaroo tendon *Result* Union in seven weeks' time Anterior and posterior molded plaster of paris splint applied

Case 8—Male, age 45 Fracture of lower third left tibia Intramedullary rolled cuff anchored with kangaroo tendon Also osteoperiosteal bone graft used in same case, with bone chips *Result* Union in 12 weeks' time Plaster encasement fixation

Case 9—Female, age 66 Fracture of left humerus Automobile accident Seen after several attempts at reduction Fracture at juncture of lower and middle thirds Beef tendon cuff anchored with kangaroo tendon *Result* Union in eight weeks' time Thomas arm splint fixation

Case 10—Male, age 56 Rather heavy, obese type Fracture of middle third right femur Fracture reduced, Thomas splint and later plaster encasement Fracture was treated in this manner for over one year, with a resulting nonunion and no callus formation whatever

At the end of one year, an open reduction was undertaken by Drs J Duffy Hancock and Ben Wilson Smock, Louisville, Ky The ends of the bone were cleaned of all fibrous material and exudate, approximated and retained by an intramedullary beef tendon splint Roentgenologic examinations made at regular intervals showed the bones to be in excellent apposition, with no callus formation The leg was reopened at the end of four months and the fracture reduced and splinted with a beef bone intramedullary graft There was no trace of the beef tendon found at the time the leg was opened up four months after its application, to the femur

Result—Six months after the beef bone graft had been employed, the patient was found to still have a false joint, with nonunion He is now able to get about with the use of a cane

COMMENT—The beef tendon splint served its purpose in splinting and supporting the line of fracture perfectly, and was demonstrated to have been absorbed at the end of four months We feel that it worked perfectly as a splint for open bone reduction, that it was in no way to blame for the nonunion, as previous treatment and subsequent treatment using different methods were also failures in effecting the uniting of this fracture

Appreciation is made to Dr Ralph O Clock, of the Davis and Geck Company of New York, for his assistance in the preparation of this material and for donating a supply sufficient to enable us to reach a conclusion regarding its availability

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BRIEF COMMUNICATIONS AND CASE REPORTS

MALIGNANT TRANSFORMATION OF A SOLITARY SIGMOID ADENOMA

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It is generally believed that there is a marked tendency for adenomata of the large bowel to undergo malignant transformation. The evidence, which is wholly indirect and circumstantial, has been questioned upon the grounds that their association may be coincidental. The case herewith reported we believe affords direct clinical evidence of such transformation, and is substantiated by pathologic sections.

Case Report—(Hospital No. 404403) J. G., male, age 45, Russian, tailor, was first seen in the Mt. Sinai Hospital Out-Patient Department in June, 1936. He had been well until ten years prior when he began to have painful, bloody bowel movements. He was told he had fissures and hemorrhoids and he was operated upon at another institution. No relief was obtained, however, for he continued to have attacks of painful, bloody diarrhea. This continued in a milder form through the ensuing years and no diagnostic therapeutic procedures were undertaken until two years prior to his admission when he began to suffer from episodes of severe constipation alternating with attacks of diarrhea, and the passage of "pus, mucus and blood." Often he would have as many as 12 movements in 24 hours. His physician, after making a roentgenologic and proctoscopic examination, told him that he had hemorrhoids, anal fissures and "catarrh of the bowel." He was admitted to another institution in January, 1936, and again an hemorrhoidectomy was performed. Several weeks later rectal bleeding recurred, and he also developed epistaxis and generalized petechiae. He was readmitted to the same hospital where blood studies revealed RBC 3,500,000, platelets 90,000, bleeding time 30 minutes, clotting time 11 minutes. He received two transfusions and had snake venom injections administered. The attacks of epistaxis and petechiae stopped, and at the time of his discharge from the hospital the platelet count had risen to 200,000. Mild, occasional rectal bleeding continued. Five months later, however, there was a recurrence of all his previous symptoms—epistaxis, petechial spots and severe rectal bleeding. He was then referred to the Mt. Sinai Hospital. It was ascertained at this time that during the past two years he had been on a diet of bread, meat and potatoes almost exclusively.

Physical Examination disclosed a chronically ill, pale, poorly nourished, middle aged male. There were numerous petechiae present over the general body surface. The liver and spleen could not be felt. There were no palpable lymph nodes. Chest negative. Urine negative. Blood Wassermann negative. Blood examination showed Hemoglobin 76 per cent, RBC 5,220,000, WBC 10,950. Differential, segmented polys 70 per cent, nonsegmented 3 per cent, lymphocytes 22 per cent, monocytes 3 per cent, eosinophiles 2 per cent. Platelets 130,000. Bleeding time $6\frac{1}{2}$ minutes, coagulation time $7\frac{1}{2}$ minutes.

Treatment with snake venom was continued for a time. The epistaxis and petechiae

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diminished but the episodes of bloody diarrhea continued and he was referred to the Rectal Clinic

Proctologic Examination—*Inspection* The peri-anal skin was normal except for a few small skin tags. *Digital* No abnormalities were noted. *Anoscopy* The anal canal showed definite evidence of scarring with obliteration of all normal landmarks. *Sigmoidoscopy* At full length a polyp the size of a large cherry was encountered. The tumor appeared normally pink in color and had the usual velvety surface seen in benign polyps. When the end of the sigmoidoscope was passed over the tumor, one obtained the impression that the tumor was soft.

Clinically the lesion was definitely benign, but as a routine measure biopsy was



FIG 1.—Photomicrograph of a typical section of the multiple biopsies showing the histologic characteristics of an adenomatous polyp

performed, three large pieces being taken from different areas. The mucosa was otherwise normal. A barium enema was reported as revealing no evidence of an organic lesion.

Pathologic Report—By Dr Paul Klemperer (No 58023) "Fragments of tissue from colon. They consist of elongated, often branching glands within an hyperemic stroma infiltrated by plasma cells and polymorphonuclear leukocytes. There are glands lined by goblet cells, but the greater number of glands are lined by high columnar epithelium with dark rod-shaped nuclei, often multilayered. Mitotic figures are seen occasionally. *Pathologic Diagnosis* Fragments of adenomatous polyp" (Fig 1)

After the negative pathologic report and the negative barium enema, it was decided to coagulate the polyp. Sigmoidoscopy was again performed and the polyp

MALIGNANT SIGMOID ADENOMA

brought into view. When the coagulating electrode was introduced the tumor slipped back beyond the reach of the sigmoidoscope. After this had occurred several times, it was inferred that the polyp was on a long pedicle. The tumor was ultimately visualized and a complete surface coagulation done. All bleeding ceased after the coagulation. Attempts at further coagulation were made at frequent intervals, but because of poor preparation the tumor could not be visualized and it was not until several weeks later that a successful sigmoidoscopy could be accomplished. At this examination, eight weeks after the first observation and biopsy, the tumor presented an entirely different appearance. It now appeared dark red in color, definitely lobulated and felt distinctly hard through the medium of the sigmoidoscope. In spite of the recent negative biopsy, the



FIG 2—Photomicrograph of a section of the subsequent biopsy, eight weeks, showing adenocarcinoma

tumor appeared so decidedly malignant, that another biopsy was immediately performed. Without awaiting the report of the pathologist, complete surface coagulation was done.

Pathologic Report—By Dr Paul Klemperer (No 58448) "The outstanding feature in the histology is the appearance of the glands. They are strikingly elongated and branching and very many are lined by low columnar cells in disorderly arrangement with large vesicular nuclei and one or two large eosinophile nucleoli. Mitotic figures are very frequent. There are other glands which are lined by high columnar cells with rod-shaped nuclei, the type cell seen in the previous biopsy. *Pathologic Diagnosis* Adenocarcinoma" (Fig 2)

The patient was admitted to the surgical service, February 8, 1937, and was operated upon by Dr A J Beller

Operation—February 24, 1937 Under spinal anesthesia, the abdomen was opened through a left rectus incision. The entire colon was palpated and found to be normal except for the sigmoid where a movable mass could be felt. The liver was apparently normal and there was no involvement of mesenteric nodes. The sigmoid was opened by a vertical incision exposing a cherry-sized, irregularly nodular, somewhat firm tumor on a pedicle about one and one-half inches long. The pedicle was ligated at its base, cut with the cautery and the tumor and pedicle removed. The sigmoid was then closed transversely. The abdomen was closed in layers. The patient made an uneventful recovery and was discharged on the thirteenth day postoperatively.

Pathologic Report—By Dr. Paul Klemperer (No. 58629) "Adenomatous polyp with early adenocarcinoma. There is no involvement of the pedicle."

The patient has been seen frequently in the Follow-Up and Rectal Clinics and was last examined January 12, 1938. He has been on a normal diet and has gained 25 pounds. There have been no evidences of petechiae or epistaxis and there have been no further episodes of diarrhea or rectal bleeding. Sigmoidoscopy as well as barium enema have been entirely negative. Blood examination: Hb 98 per cent, RBC 5,010,000, WBC 7,500. Differential: Polys 70 per cent, lymph 23 per cent, monocytes 5 per cent, eosinophiles 1 per cent, basophiles 1 per cent. Platelets 240,000, Bleeding time 1 minute, coagulation time 16 minutes. The clot retracted normally. The tourniquet test was negative.

COMMENT—We do not know with certainty how long the adenoma had been present, but feel reasonably sure that it had existed for ten years. The reasons for this are: First, the ten year history of rectal bleeding, unrelieved by two hemorrhoidectomies performed eight years apart, second, the blood dyscrasia occurred but one year prior to his admission to the Rectal Clinic and presumably did not initiate the rectal hemorrhages but rather increased the tendency to them, and third, upon removal of the tumor all bleeding ceased. The temporary complicating blood dyscrasia was at first considered to be due to avitaminosis. Consultation with the hematologist, however, established the fact that this was merely a transitory idiopathic purpura.

When we first saw this tumor the clinical appearance, through the sigmoidoscope as well as the feel imparted through the instrument, was typical of a benign adenoma. This was verified by biopsy. Realizing full well the pathologic variations that may exist in different parts of the same tumor, three large pieces were removed and each was sectioned. Eight weeks later the clinical appearance had changed to such an extent that we immediately made a clinical diagnosis of malignancy and took new sections. Our clinical diagnosis was again confirmed by the pathologist. There is but little doubt that during this short interval the transition from benign to malignant occurred. As additional evidence of the very early stage of the malignancy we have the fact that the pedicle, which was sectioned in several places, failed to show any neoplastic cells.

It is possible that the coagulation may have been the exciting trauma which resulted in the profound change. This of course is open to question, but in no way detracts from the fact that a malignant transformation did occur in a proven benign solitary adenoma.

INTUSSUSCEPTION OF THE APPENDIX

FREDERICK CHRISTOPHER, B S , M D

EVANSTON, ILL

UP TO 1922, Szenes¹ was able to collect 58 cases of intussusception of the appendix from the literature. In 1927, Huddy² added a case of his own, three which apparently had been overlooked by Szenes, and seven others. Both Szenes and Huddy seem to have overlooked the cases of Curiy and Shaw,³ and Farr.⁴ Since 1927, the cases of Anzilotti,⁵ Withrow,⁶ Hamilton,⁷ MacDermott,⁸ Mitchell,⁹ Esaw,¹⁰ Coopersnail,¹¹ and Bosi¹² have been published. To these should probably be added the cases of Spurney and Nyquist,¹³ and Hipsley.¹⁴ In all, some 80 cases of intussusception of the appendix have been reported.

As pointed out by Huddy, and confirmed by subsequent reports, "by far the greater number of cases arise in young children." The invagination of the appendix may be chronic or subacute and vomiting and loss of weight have been noted. A sequel to intussusception of the appendix occurs when the inverted mass is carried forward by peristaltic action and drags the ileocecal valve along the colon producing a major intussusception. Moschowitz¹⁵ observed that cases of intussusception of the appendix had a "more or less protracted history of repeated attacks of severe abdominal cramps occurring intermittently with periods of well being." Palpable tumor and blood in the stool have been noted. Where the appendix may be disinvaginated, its simple removal should suffice to cure. In many cases, however, this cannot be accomplished and it has become necessary to resect the cecum.

Case Report—P. S., age 9, was admitted to the Evanston Hospital March 15, 1938. Seven years previously (September 14, 1931) the patient was sent to the Evanston Hospital by Dr. C. A. Aldrich with a diagnosis of intussusception. At that time he had had cramp-like pains which came on at 20 minute intervals all during one night. The pain was relieved following an enema. Doctor Aldrich felt that there had been an intussusception which had reduced following the enema. For a number of years previous to the second admission to the hospital the patient had had attacks of abdominal pain which were never definite enough to call appendicitis. Three weeks before admission he had an attack of generalized abdominal pain with vomiting. After a few hours the pain localized in the right lower quadrant. He experienced pain in the abdomen as recently as the day before admission. Physical examination was negative save for rather marked tenderness and some rigidity in the right lower quadrant. The leukocyte count at this time was 7,000, although it had been 10,000 a few days previously. The urine was normal.

Operation—March 16, 1938. The appendix was found to be at least one-half inch in diameter and very firm and edematous. There were some petechial hemorrhages on its surface. It was attached to the cecum at almost a right angle. At the junction of the appendix and the cecum a smooth confluence of serosa of cecum and appendix presented. This was due to old adhesions. The adhesions were dissected free and there was then disclosed a cleft running around the base of the appendix indicating an invagination of the appendix into the cecum. This finding was confirmed by feeling, through the opposite wall of the cecum, the protrusion for one-half to three-quarters of an inch of intussusception into the lumen of the cecum. By pressure on this protrusion into the cecum and slight traction on the appendix the intussusception was reduced. A con-

stricted ring on the appendix marked the furthest advance of the intussusception. The appendix was removed after catgut ligation and linen pursestring inversion. The McArthur-McBurney incision was closed without drainage and the boy made a rapid recovery (Fig 1).

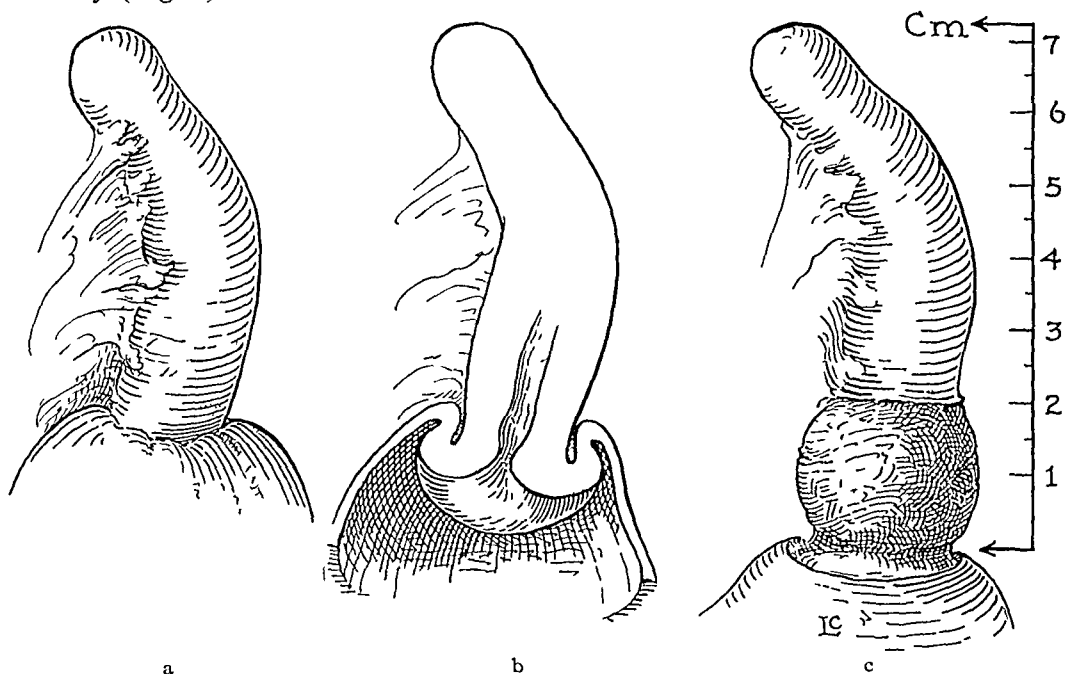


FIG 1—Intussusception of the appendix. (a) Condition found at operation. At the junction of the appendix and the cecum were old adhesions which are not shown in this drawing. (b) Schematic representation of the intussusception of the appendix into the cecum. The intussusceptum could be palpated through the wall of the cecum. (c) Appearance of the appendix after the intussusception was reduced.

SUMMARY

(1) Intussusception of the appendix is uncommon, some 80 cases being recorded in the literature.

(2) It occurs chiefly in young children, the diagnosis is difficult, the treatment may require resection of the cecum.

(3) A case of intussusception of the appendix is reported.

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A PRINCIPLE TO BE CONSIDERED IN TRANSPLANTING COSTAL CARTILAGE FOR REPAIRING DEFICIENCIES OF THE NASAL SKELETON

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It is the purpose of this paper to point out a method for more anatomically restoring loss or deficiencies in the bony and cartilaginous framework of the nose. The principle is of wide application and although suggested in part, prior to this communication by Gillies and McIndoe,¹ has not been clearly formulated in its entirety for those interested in reconstructive surgery of the face.

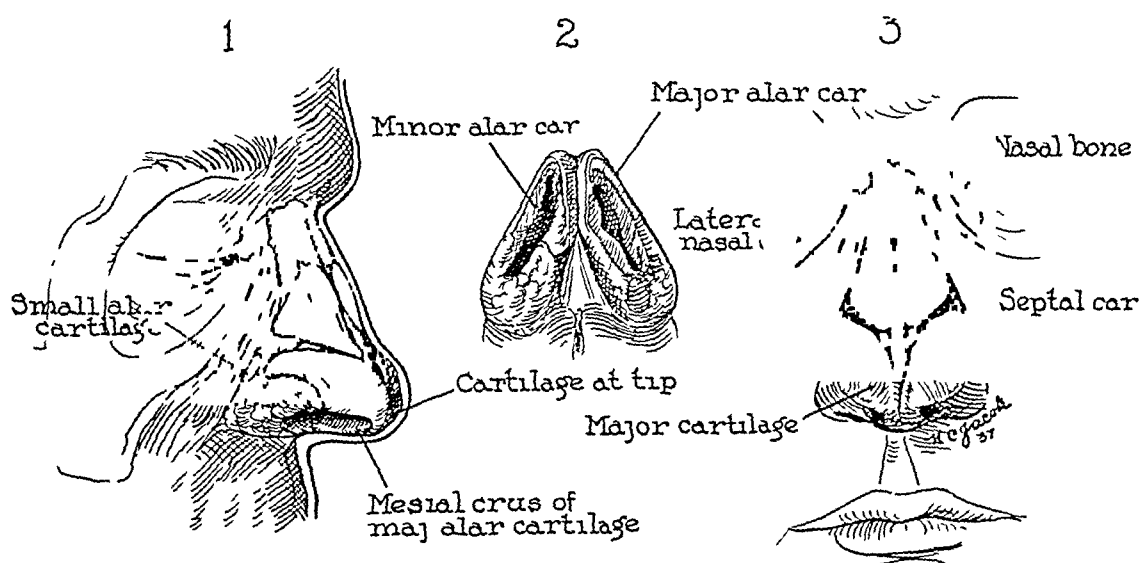


FIG 1.—Normal nasal skeleton. Notice the manner in which the septal and alar cartilages are hinged. This allows mobility and yet retains form.

The nose consists of a skeleton of bone and cartilage, covered exteriorly by skin and fat and on the inside by mucous membrane. It is in effect a tent, the ridgepole of which is made up superiorly by the midline junction of the nasal bones, in midportion by the dorsal edge of the cartilage of the nasal septum, and at the tip by the folded, opposed edges of the major alar cartilages supported on the cartilage of the septum below. The pitched roof of the tent is supported on either side by the nasal bones above and the lateral and major alar cartilages below (Fig 1).

This framework may be damaged, or partially or completely lost. The more common causes of such deficiencies in the supporting nasal skeleton are infection, trauma, and congenital failure of development. New growths usually destroy skin and mucous membrane as well.

Such a loss or disarrangement of bone and cartilage allows the skin covering to sag inward. This falling in of the nose changes its contour and in so doing changes the entire appearance of the face. It may, by decreasing the anteroposterior diameters of the nasal passages, seriously interfere with nasal

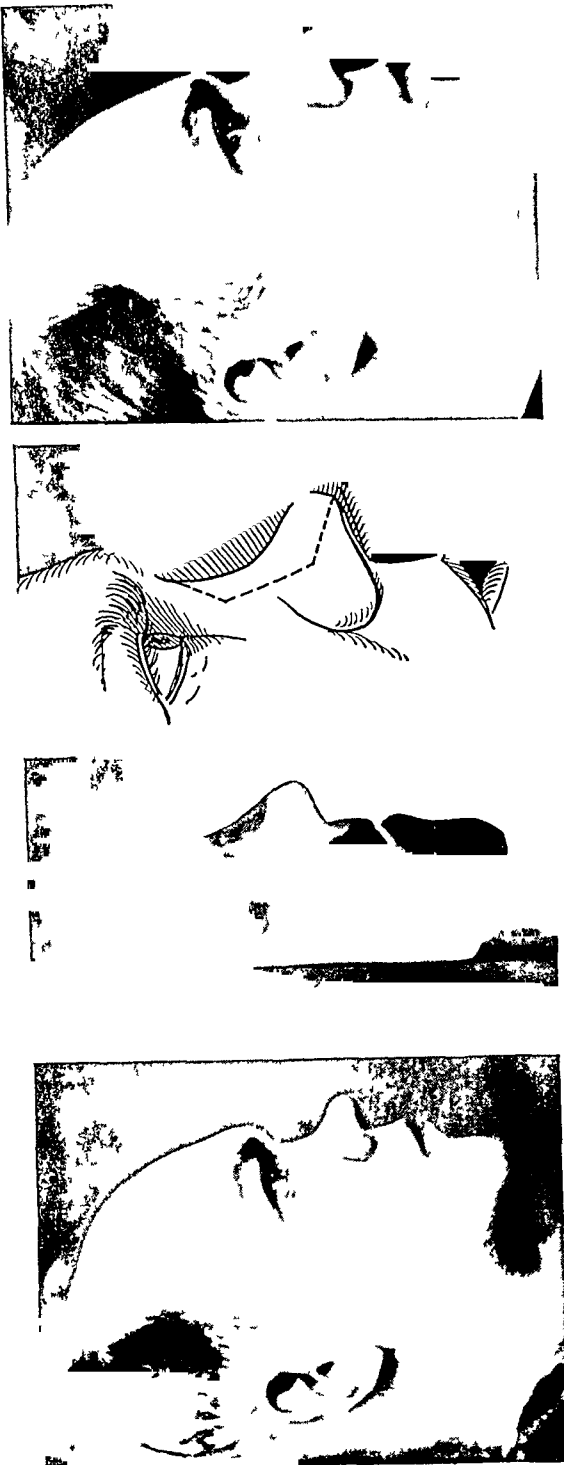


FIG 2—Falling in of dorsum of nose due to destruction of cartilage by pyogenic abscess. Nasal breathing impossible when recumbent. A hinged cartilage transplant corrected the appearance and provided a sufficient airway.



FIG 3—Partial loss and derangement of cartilaginous skeleton from compound fracture. Obstruction to breathing improved by submucous resection. Contour restored by hinged cartilage transplant.

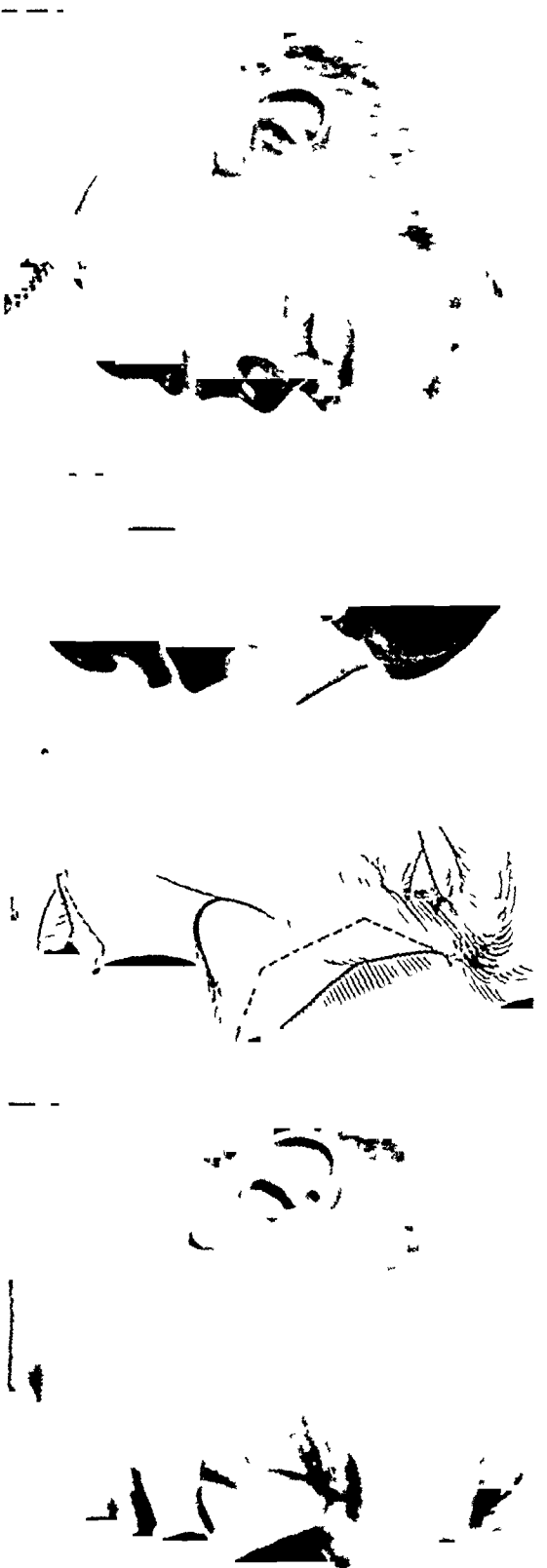


FIG. 4.—Perforation and loss of both cartilage and bone following compound telescoping fracture of frontal, nasal and maxillary bones. By a series of operations the open bite was corrected, the forehead depressed and the soft tissues rearranged and the nose lengthened. The nose was then brought to its final appearance on the right side by a cartilage transplant.

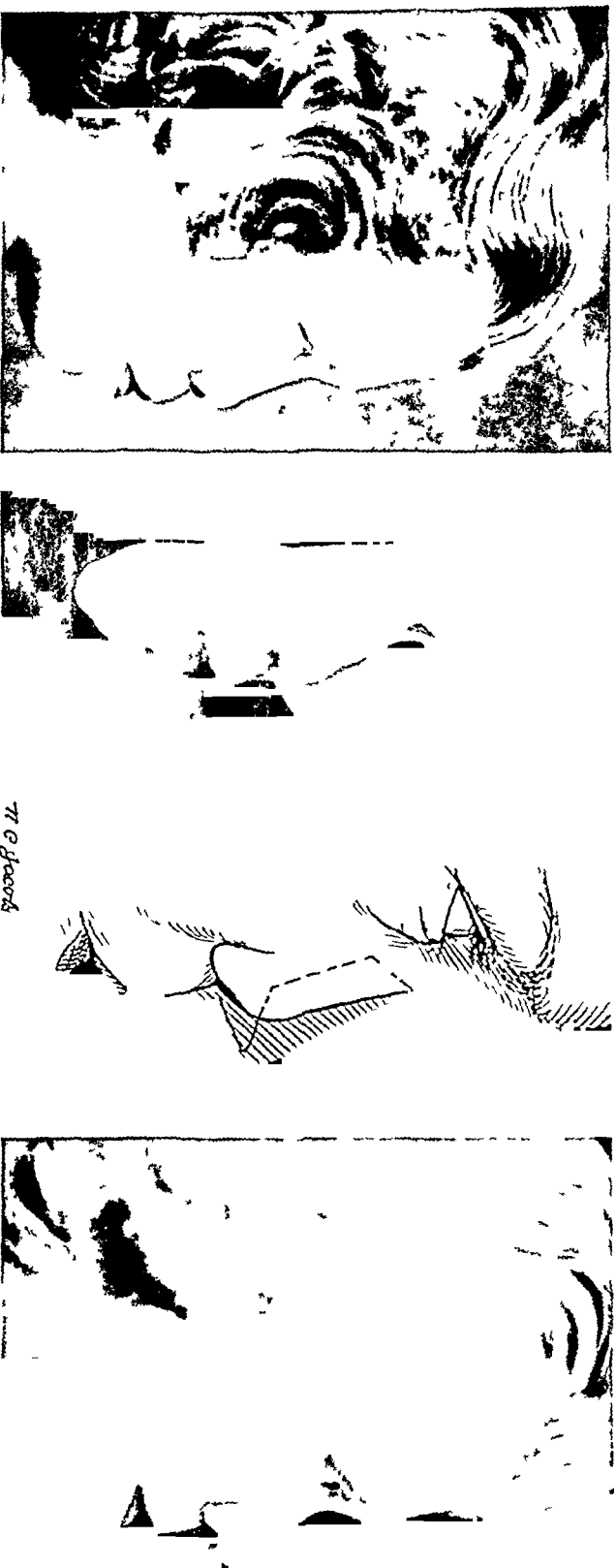


FIG. 5.—Marked retrocession of nose due to congenital absence of cartilaginous skeleton. Final appearance obtained in four stages: (1) Advancement of soft tissues, (2) lengthening soft tissues of columella, (3) an "L" shaped cartilage transplant to stretch the nasal skin still further forward, and (4) after some months, a hinged transplant to construct the nasal tip.

respiration (Fig 2) Thus loss of the nasal skeleton in part may damage both the appearance and function of the nose Any method for correcting such a condition should attempt to improve both, and in effecting this the restoration should, without question, follow as nearly as possible the normal anatomic make-up

For supplementing the nasal skeleton various substances have been employed Among these are rubber, paraffin, ivory, celluloid, various metals,

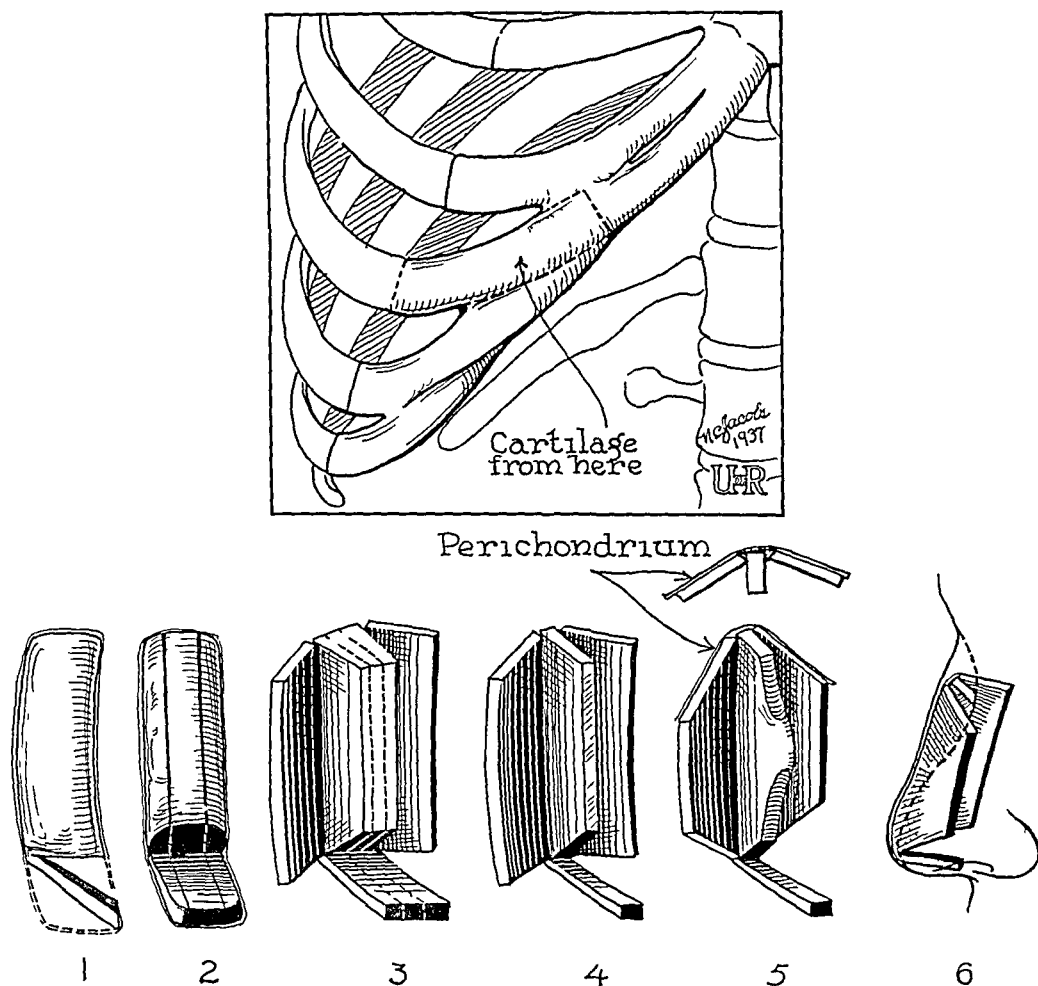


FIG 6—Diagrammatic representation of the construction of a hinged costal cartilage transplant

cellulose plastics, heterogenous and autogenous bone and cartilage I think it is safe to say that the human body tolerates foreign material poorly Moreover, individuals are biologically so different that an inert substance which may persist in one, without an attempt of the body to cast it off, will not be well tolerated by another In the present state of our knowledge concerning the exceedingly complex question of tissue transplantation, we feel that it is best to employ only autogenous material, and of these costal cartilage is better, on the whole, than bone It can be more easily shaped to a desired form than bone and it exists on very little nourishment Thus over a period of time bone may be absorbed but cartilage atrophies very little when transplanted subcutaneously and usually maintains its shape well

In some instances a depression of the dorsum of the nose following trauma is not a result of actual cartilaginous loss but of disarrangement. In these cases there is usually a fracture of the cartilaginous skeleton with displacement downward in such a way as to partially obstruct the nasal airways. In some of these the framework can be rearranged in approximately normal fashions as suggested by New,² Straith³ and others, but in a majority of instances it is necessary to perform a more or less modified submucous resection to improve breathing, and then transplant cartilage to the dorsum to restore contour (Figs. 3 and 4).

In loss of substance from septal abscess, there must, of course, be a reconstruction, which means a transplant. The same is true in congenital failure of formation of the framework (Fig. 5).

Operative Technique—The method which we have gradually evolved is a rather crude attempt to replace not only the dorsal edge of the septal cartilage but the alar cartilages as well. Instead of placing a long strut of cartilage along the dorsum, appropriately shaped to fill in the depression, as is the usual practice, a section of costal cartilage is removed with its perichondrium intact. This section is selected with the curve or straight line desired for the dorsal line of the nose. If a columellar support is needed, the first cut provides for a vertical post hinged to the main mass. Parallel longitudinal cuts are made on the edge opposite that selected for the dorsal ridge. These cuts go down or almost to the perichondrium and the thin wings are fractured outward so that they remain hinged by perichondrium. The median mass is thinned and shaped to a pattern previously determined from a cast of the face upon which the desired nose has been built in clay and halt removed. The wings are thinned and shaped (Fig. 6).

Modeling such a transplant is a more difficult task than making a simple long strut, and it requires a wider opening to allow its introduction under the nasal skin. We make an incision usually just inside the mucocutaneous line of the alar and carry it across the columella at its junction with the nasal tip. This allows a clear view under the skin of the nose and easy introduction of the transplant. A small tunnel can be made downward for the columellar prop if it is necessary.

Such a transplant we believe is superior to the usual cantilever strut. If carried out according to indications and well conceived preoperative plans, it produces more normal appearing side walls of the nose and allows a larger airway below, because the nasal lining is not held downward by a large mass of cartilage designed merely to rest upon it in its depressed position.

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AN IMPROVEMENT IN THE APPLICATION OF BONE PLATES

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THIS is not a plea for the application of plates to fractures, simpler measures of retention should be used where they suffice. Nevertheless, there does seem to be a small percentage (about 5 per cent in my experience) where some form of internal fixation is required, and in some of these a properly applied plate offers a satisfactory means of maintaining immobilization and contact at the fracture line. But if a plate is to be employed the mechanics of its application should be as perfect as possible. Asepsis and satisfactory reduction of the fracture are taken for granted, as in all open bone surgery.

Our present concern being with the mechanics of the application of plates, six desiderata appear to be indispensable

FIG 1

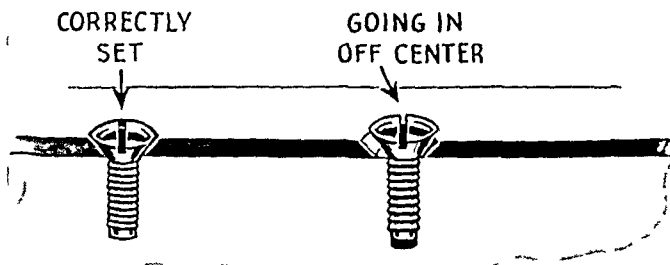
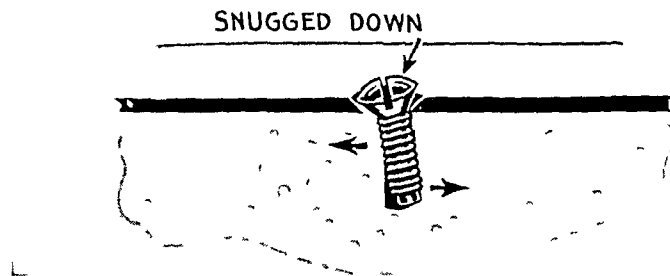


FIG 2



FIGS 1 and 2—Show a screw properly set and one introduced off center, which causes side pressure, resulting in eventual loosening of the screw

- 1 A strong plate of noncorroding metal
- 2 Metal type of screws, self-tapping, same material as the plate, to prevent electrolysis *
- 3 Correct size drill for the screw employed—same as the root diameter of the screw
- 4 Drill-holes perfectly centered in the hole of the plate
- 5 At least half of the screws long enough to engage the opposite cortex
- 6 Screws snugged in place but not tightened excessively

Submitted for publication February 14, 1938

* Experiments are under way to prove the superior holding qualities of screws with coarser and deeper threads, designed for uniting sheet metal, bronze, monel metal, bakelite, etc, and will be reported shortly

APPLICATION OF BONE PLATES

Considerable work has been done by Zierold, Leriche and Policard, Jones and Policard, Sherman and more recently by Venable, Stuck and Beach in improving the composition of plates and screws, but no one has offered a satisfactory means of enabling the operator to center his drill-holes correctly in the holes of the plate. The bevel of the head of the screw fits the bevel of the hole in the plate so that as the screw is tightened down it is forced into the center. The first hole makes no difference because the plate is still free to move about, but as soon as one screw is snugged in place the plate is anchored, and unless subsequent drill-holes are perfectly centered terrific side pressure is going to be exerted because the plate cannot give. This side pressure un-

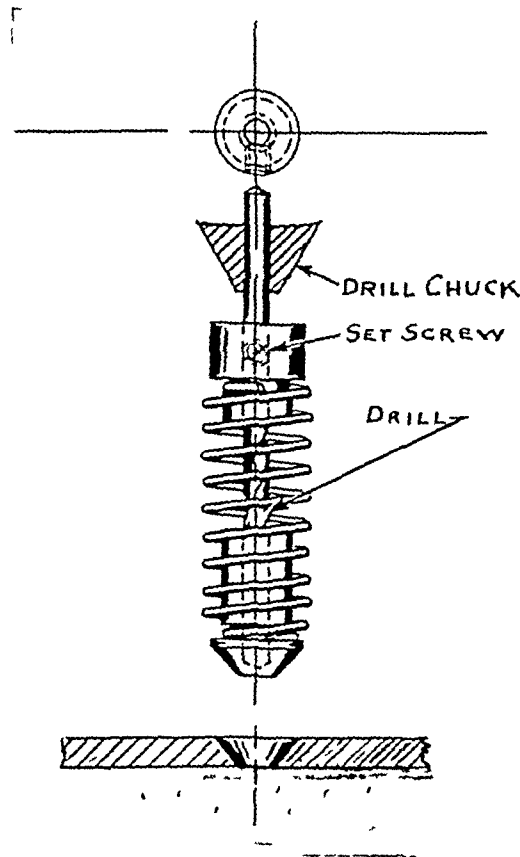


FIG. 3—Shows a drill centering jig, constructed to overcome the tendency to introduce the screw eccentricity.

doubtedly accounts for occasional fractures through the drill-holes, and more often for premature loosening of the screws as the bone retreats before the extreme side pressure of the screw when it is placed eccentrically (Figs 1 and 2).

To overcome this difficulty a small drill-centering jig has been devised, and used a sufficient number of times to justify the conclusion that it works as well practically as theoretically (Fig 3).

The jig consists of two buttons, the upper one containing a set-screw which secures it to the drill. The lower one is beveled to fit the bevel of the hole in the plate. Between the two is a coil spring which is not attached to the buttons but encircles them loosely in a narrow groove. This spring

should be just rigid enough to withstand a sufficient pressure to keep the lower button firmly in the hole of the plate as the drill is being started, so that it is kept definitely in the center of the hole. The jig must be placed at such a height on the drill that the point does not protrude through the lower button, for if the point does protrude the jig cannot exercise its centering action. Obviously, too, a correctly sharpened drill-point will not tend to wander as will one that is ground incorrectly and asymmetrically.

Properly applied, a plate may be depended upon to give perfect immobilization at the fracture line, and external splints need be employed only for minimal protection.

FINNEY-HOWELL RESEARCH FOUNDATION, INC

Announcement has been made by the Finney-Howell Research Foundation, Inc., that all applications for fellowships for next year must be filed in the office of the Foundation, 1211 Cathedral Street, Baltimore, Maryland, by January 1, 1939. Applications received after that date cannot be considered for 1939 awards, which will be made the first of March, 1939.

This Foundation was provided for in the will of the late Dr. George Walker of Baltimore for the support of "research work into the cause of causes and the treatment of cancer." The will directed that the surplus income from the assets of the Foundation together with the principal sum should be expended within a period of ten years to support a number of fellowships in cancer research, each with an annual stipend of two thousand dollars, "in such universities, laboratories and other institutions, wherever situated, as may be approved by the Board of Directors."

Ten such fellowships were awarded in 1938.

Fellowships carrying an annual stipend of \$2000 are awarded for the period of one year, with the possibility of renewal up to three years, when deemed wise by the Board of Directors, special grants of limited sums may be made to support the work carried on under a fellowship.

Applications must be made on the blank forms which will be furnished by the Secretary or any member of the Board of Directors.

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